Strategies to Eliminate HCV and Identify Patients Most at Risk of Developing HCC in FL

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Schiff Center for Liver Diseases

Internal Medicine, Biomedical Engineering, Public Health Sciences and Microbiology/Immunology

American Liver Foundation National Board of Director

Editorial Board: Hepatology and Journal of Infectious Diseases

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

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MIAMI CFAR
MIAMI CENTER FOR AIDS RESEARCH

Learning Objectives

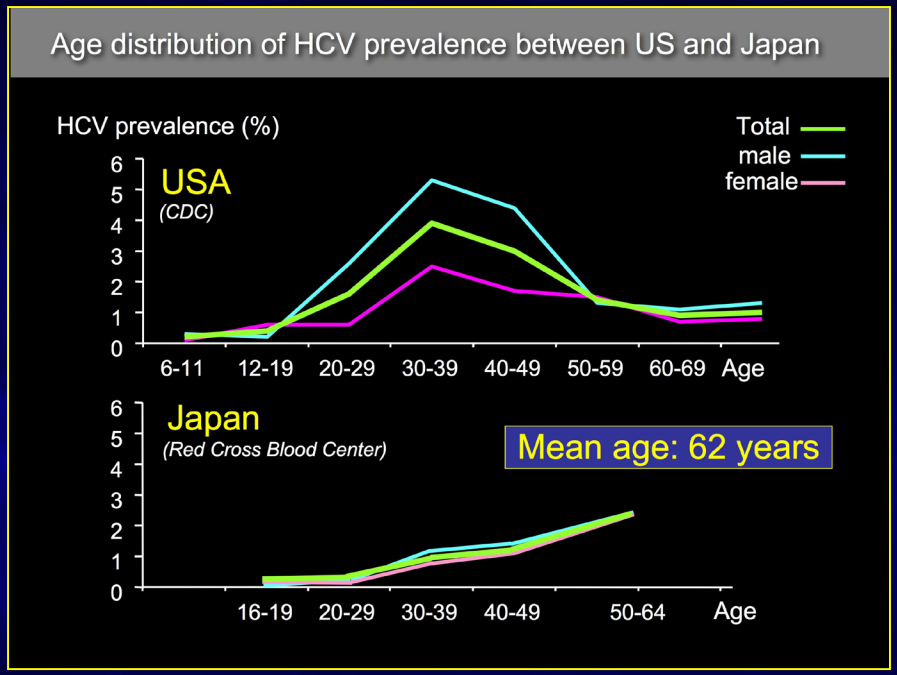
- To understand HCV epidemiology with changes from the opioid epidemic
- To understand the care cascade involving both screening and treatment for HCV
- To understand liver disease progression and risk of developing HCC from HCV

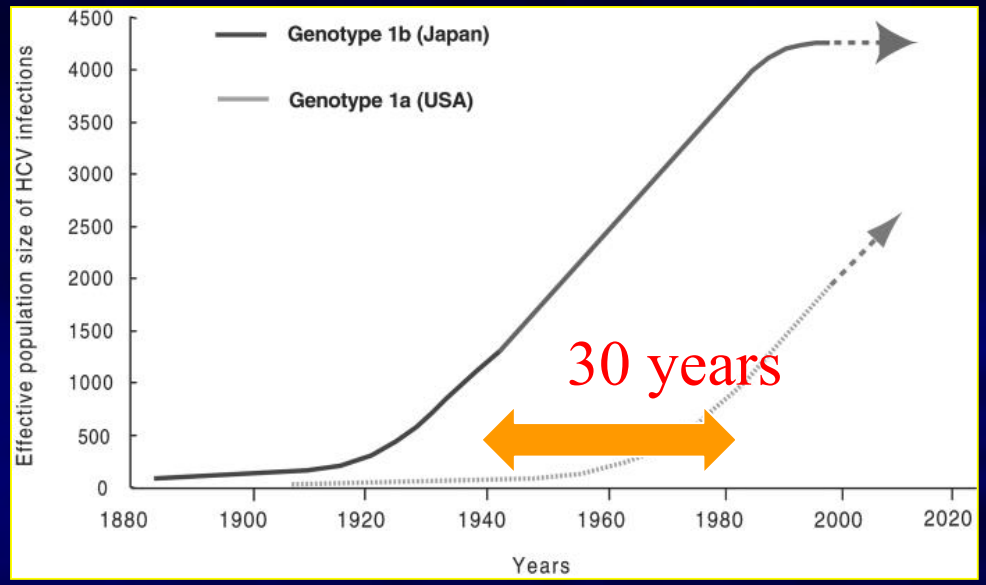
HCV Induced HCC

A comparison of the molecular clock of hepatitis C virus in the United States and Japan predicts that hepatocellular carcinoma incidence in the United States will increase over the next two decades

Yasuhito Tanaka*†‡, Kousuke Hanada§, Masashi Mizokami†, Anthony E. T. Yeo*¶, J. Wai-Kuo Shih*, Takashi Gojobori§, and Harvey J. Alter*

(Tanaka et al., *Proc Natl Acad Sci U S A.* , 2002)

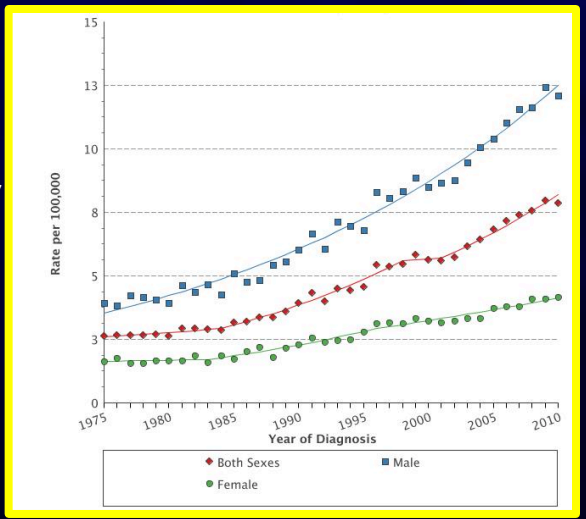




The growth of the US HCV genotype 1a-infected population occurred around 1960, at least 30 years later than the widespread introduction of genotype 1b into the Japanese population

⇒ High incidence of HCC in Japan

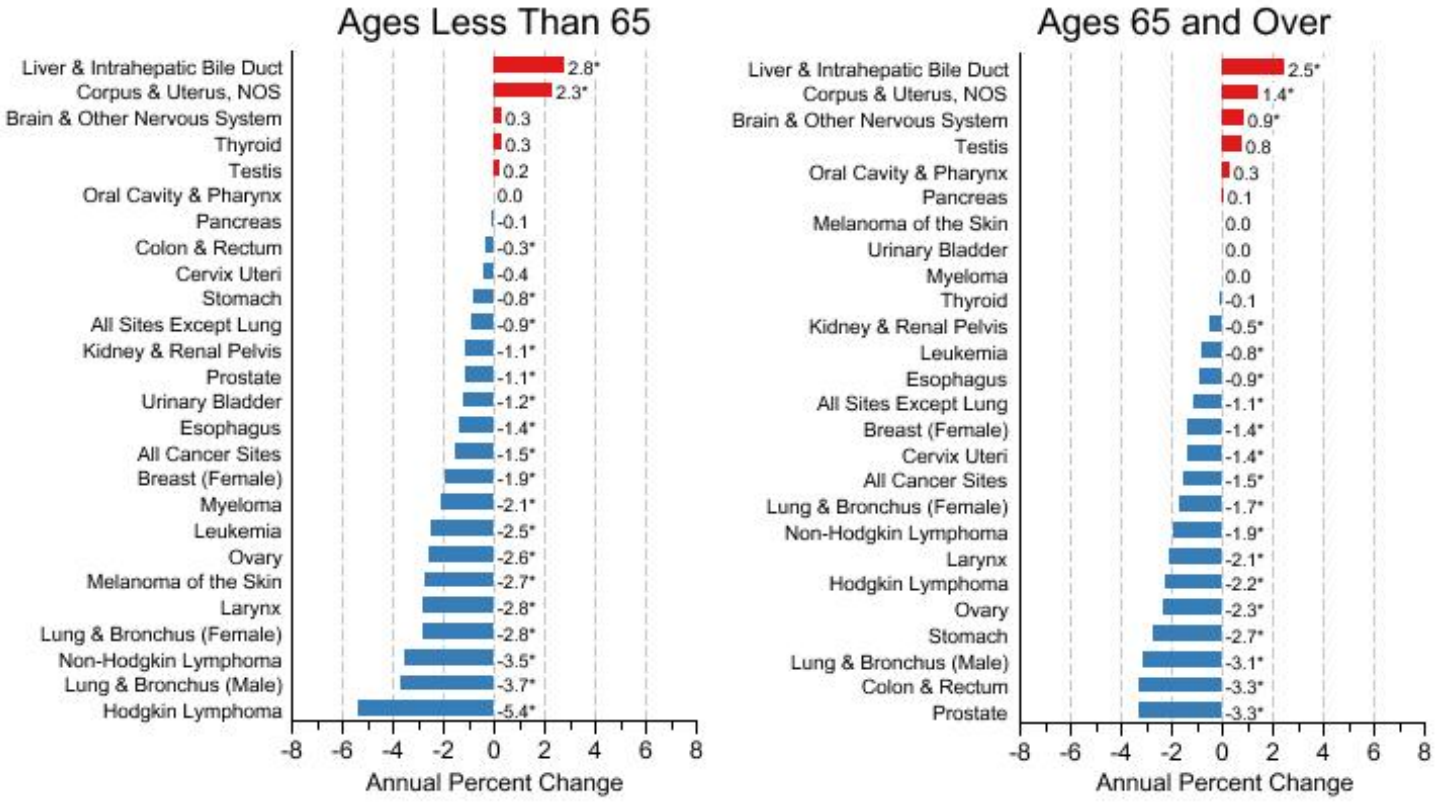
Hepatocellular Carcinoma Incidence, U.S., 1975-2010



HCC in the U.S.

Figure 1.6

Trends in US Death Rates by Age Group and Primary Cancer Site 2006-2015



Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.
Underlying rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).
For sex-specific cancer sites, the population was limited to the population of the appropriate sex.
* The APC is significantly different from zero (p<.05).

Why is HCC Incidence Rising?

Increasing prevalence of patients with cirrhosis

- Rising incidence of cirrhosis
  - HCV (main reason)
  - HBV
  - Other (?NAFLD/insulin resistance)
- Improved survival of patients with cirrhosis

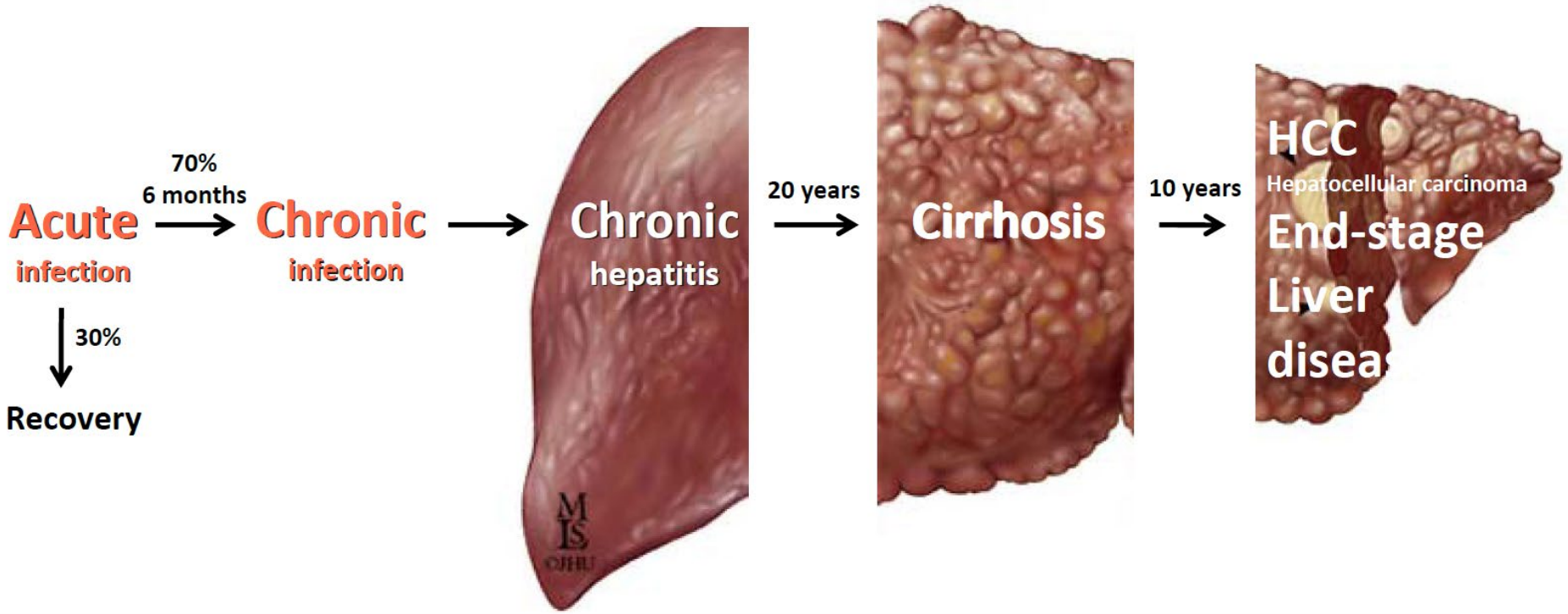
El-Serag HB, Gastroenterology 2004

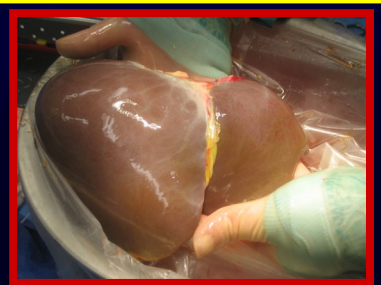
Cirrhosis in the U.S.

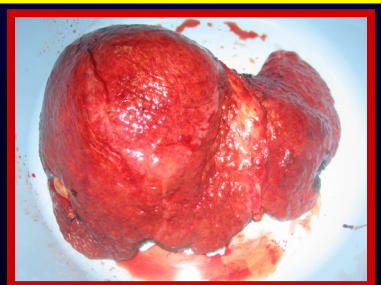
- Approximately 630,000 with cirrhosis
- 69% of Americans with cirrhosis are unaware of the diagnosis
- Cirrhosis increasing in incidence
- Incidence increases with age
- No approved therapy for cirrhosis and liver fibrosis

Beste et al., Gastroenterology 2015 & Scaglione et al., J. Clin. Gastro. 2015

HCV disease progression

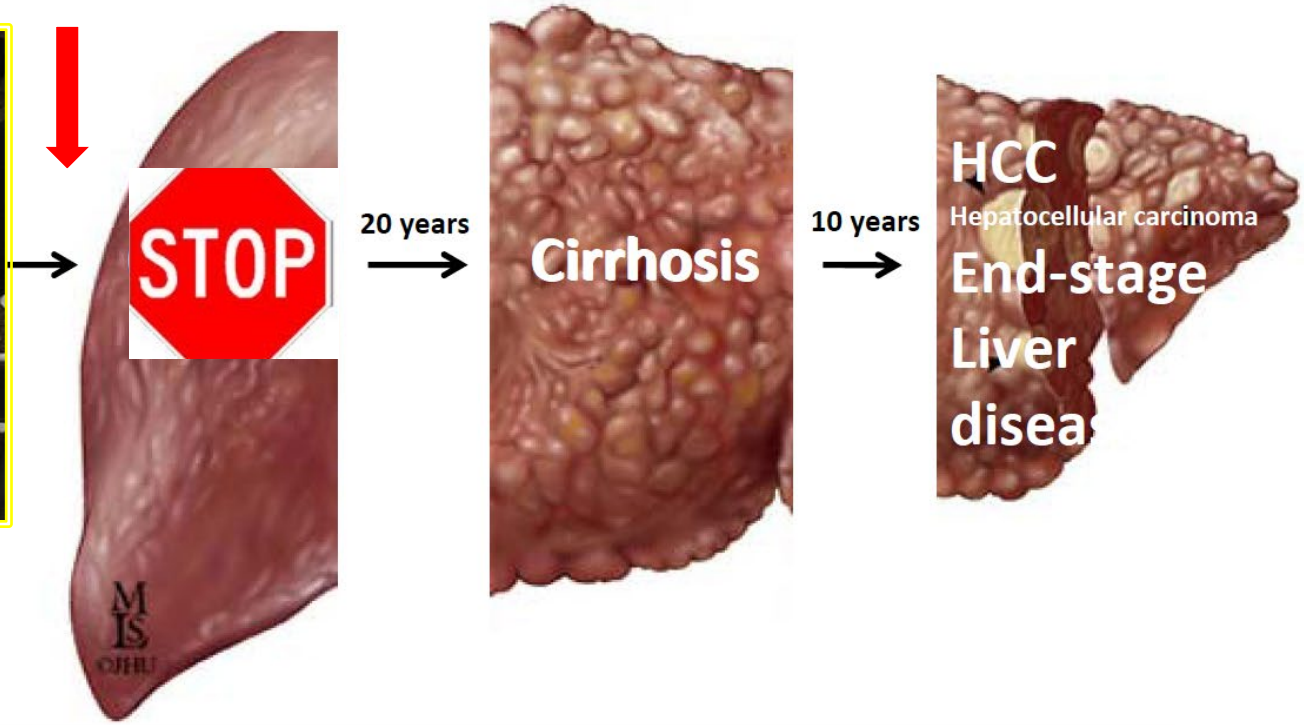


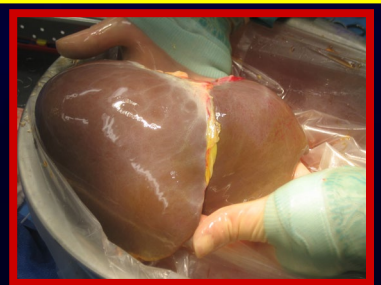


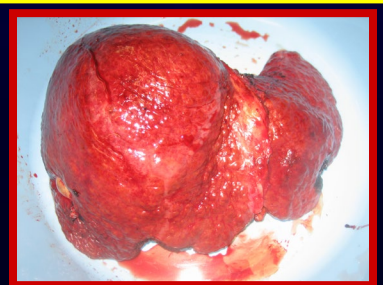


HCV disease progression

HCC Prevention/Early Detection Program







Current State of HCV Epidemic

*"**Annual HCV-associated deaths**" in the US "have surpassed the total number of deaths linked to the other **60** nationally notifiable infectious diseases combined." What's more, these "numbers are almost certainly a marked **underestimate**, Holmberg said, since, in a well-characterized cohort of HCV patients, only about one in five patients who died had the disease listed on the death certificate." Overall, mortality from HCV "continues to rise in the US" despite "dramatic improvements" in how the disease is treated.*

Scott Holmberg, MD, MPH, of the CDC's Division of Viral Hepatitis in Atlanta (ID Week meeting, October 14, 2015)

FL Opioid Epidemic

Session E:

Closing the Gap (Cont)

Grand Ballroom B

Chairpersons and Discussants:
Linda Chang, MD, University of Maryland School of Medicine
Man Charurat, PhD, Institute of Human Virology, University of Maryland School of Medicine

1:30 Elana Rosenthal, MD, Institute of Human Virology, University of Maryland School of
Collocation of HCV and OUD Treatment: The ANCHOR Study

1:50 Carlos del Rio, MD, Emory University
Integrating care for opioid use disorders to tackle ID epidemics

2:10 Glen Treisman, MD, PhD, Johns Hopkins University
The opiate epidemic-how we got here and how do we get out

2:30 Emmanuel Thomas, MD, PhD, University of Miami
IDU, HIV and Viral Hepatitis in Florida: Challenges and Opportunities

2:50 Panel Discussion

Coffee Break, 3:10 PM - 3:30 PM Grand Prefunction

Session F:

Lifetime Achievement Award Mini-Symposium

Grand Ballroom B

Chairpersons and Discussants:
Robert Mahley, MD, PhD, Gladstone Institutes
Henry Masur, MD, US National Institutes of Health Clinical Center

3:30 Robert Gallo, MD, Institute of Human Virology, University of Maryland School of Mec
Introduction to Lifetime Achievement Awards

Speaker Schedule

Thursday, October 3, 2019 - Zero Transmission

Session A:

Responses to HIV/AIDS Epidemic

Grand Ballroom B

Chairpersons and Discussants:
Shyam Kottilil, MBBS, PhD, Institute of Human Virology, University of Maryland School of Medicine
Salim Abdool Karim, MBChB, PhD, DSc, Centre for the AIDS Programme of Research in South Africa (CAPRISA)

9:00 Robert Gallo, MD, Institute of Human Virology, University of Maryland School of Medicine
Welcome, Session Comments

9:10 ADM Brett P. Giroir, MD, Assistant Secretary for Health, US Department of Health and Human Services **A-101**
Special Lecture: Ending the HIV Epidemic: A Plan for America

9:45 Q&A

9:55 Anthony Fauci, MD, Director, US National Institute of Allergy and Infectious Diseases **A-102**
Special Lecture: HIV in 2019: Optimizing the HIV Treatment and Prevention Toolkits

10:30 Q&A

Coffee Break, 10:40 AM - 11:00 AM Grand Ballroom A

11:00 Carl Dieffenbach, PhD, Division of AIDS, US National Institute of Allergy and Infectious Diseases **A-104**
Special Lecture: Epidemic Control and Beyond: What Will it Take to Truly End the HIV Epidemic

11:35 Q&A

11:45 Salim Abdool Karim, MBChB, PhD, DSc, Centre for the AIDS Programme of Research in South Africa (CAPRISA)
Closing Remarks

Lunch Break, 11:50 AM – 1:00 PM

Session B:

HIV/AIDS Prevention Strategies

Grand Ballroom B

Chairpersons and Discussants:
Mario Stevenson, PhD, University of Miami
Ken Mayer, MD, The Fenway Institute

1:00 John Brooks, MD, US Centers for Disease Control and Prevention **B-101**
Syringe Service Programs: Venues for Comprehensive Harm Reduction

FL Opioid Epidemic

-Drug overdose deaths more than doubled from 2014 (2,175 deaths) to 2016 (4,672 deaths).

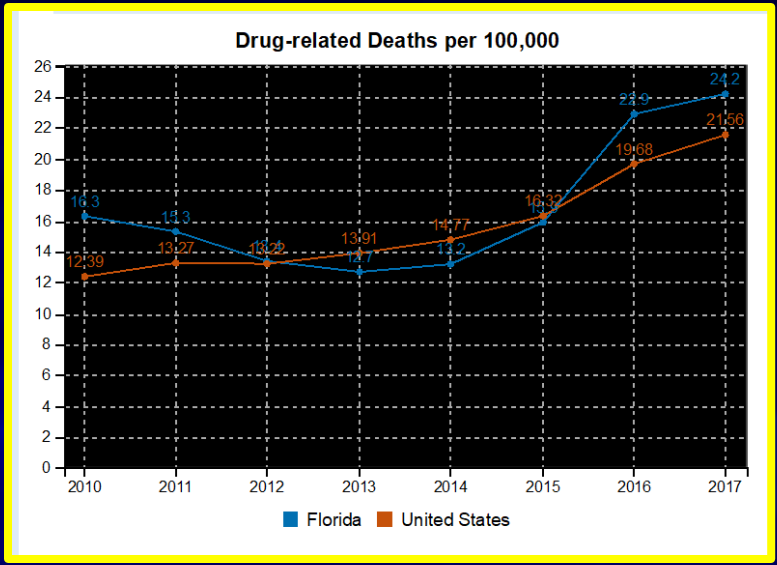
-Florida declared opioid abuse a public health emergency in 2017 with approximately $27 million in federal funds for drug treatment and prevention.

-Florida recently legalized syringe services programs through the The Infectious Disease Elimination Programs bill but prohibited the use of federal, state or local funding for any site (June 2019).

-Challenges in the state have hampered progress with addressing the opioid epidemic and transmission of communicable diseases

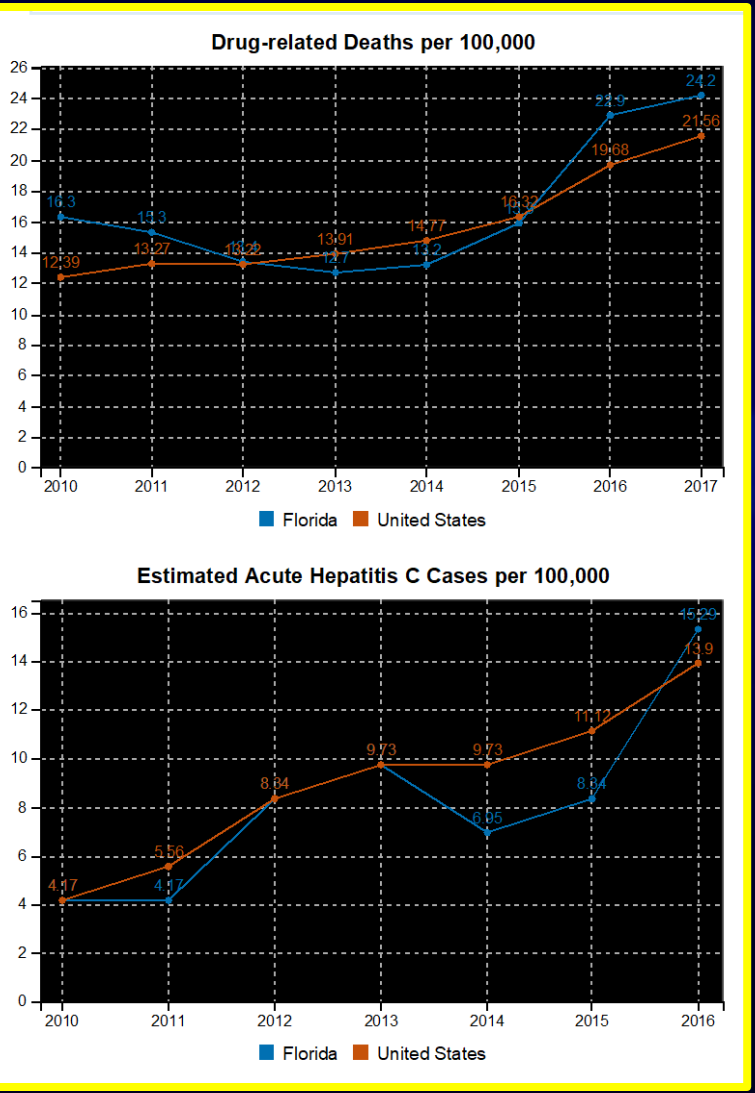
(no funding for SSPs, increasing HCV transmission, etc.).

Opioid Deaths and HIV/HCV



https://opioid.amfar.org/FL

Opioid Deaths and HIV/HCV



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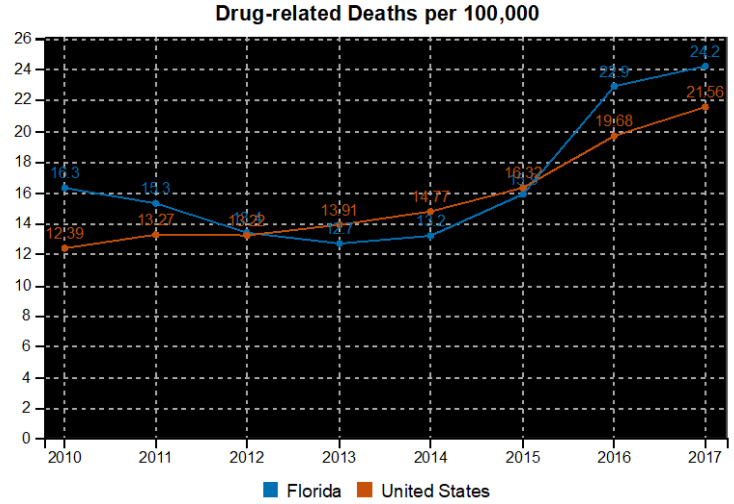
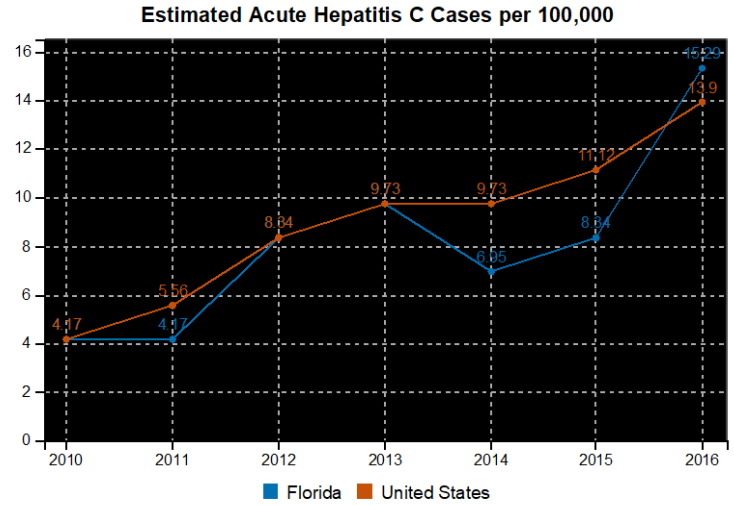
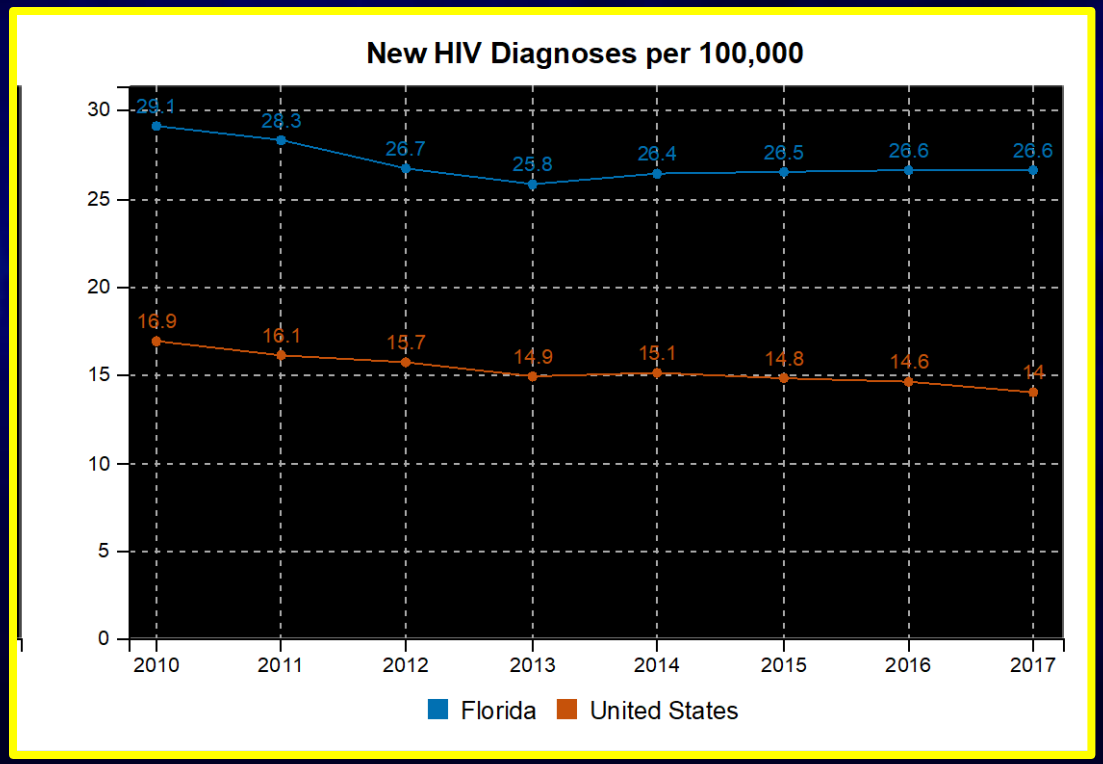
Opioid Deaths and HIV/HCV



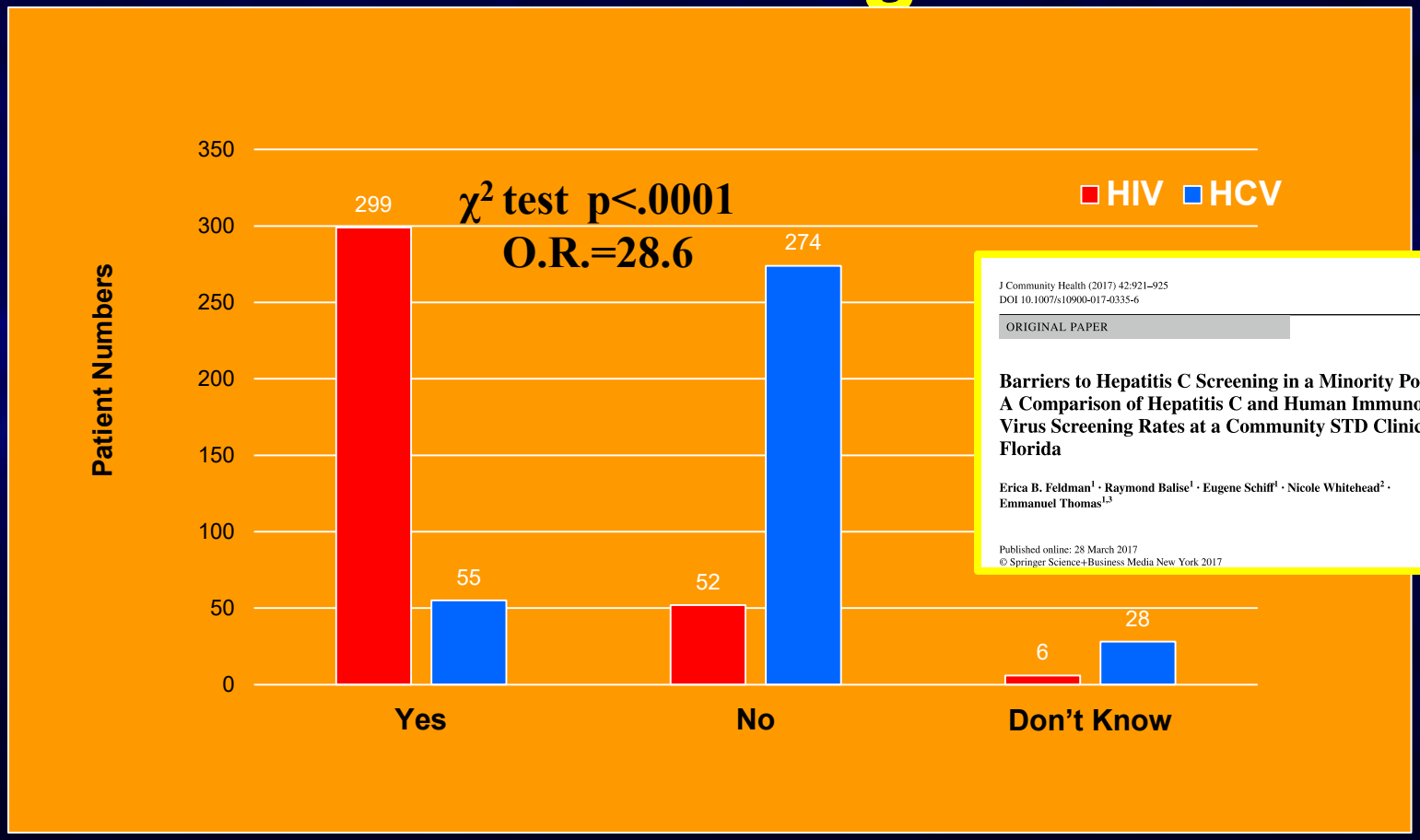




https://opioid.amfar.org/FL

HCV Testing History Data to Support Increased HCV Testing

N=357



J Community Health (2017) 42:921–925
DOI 10.1007/s10900-017-0335-6

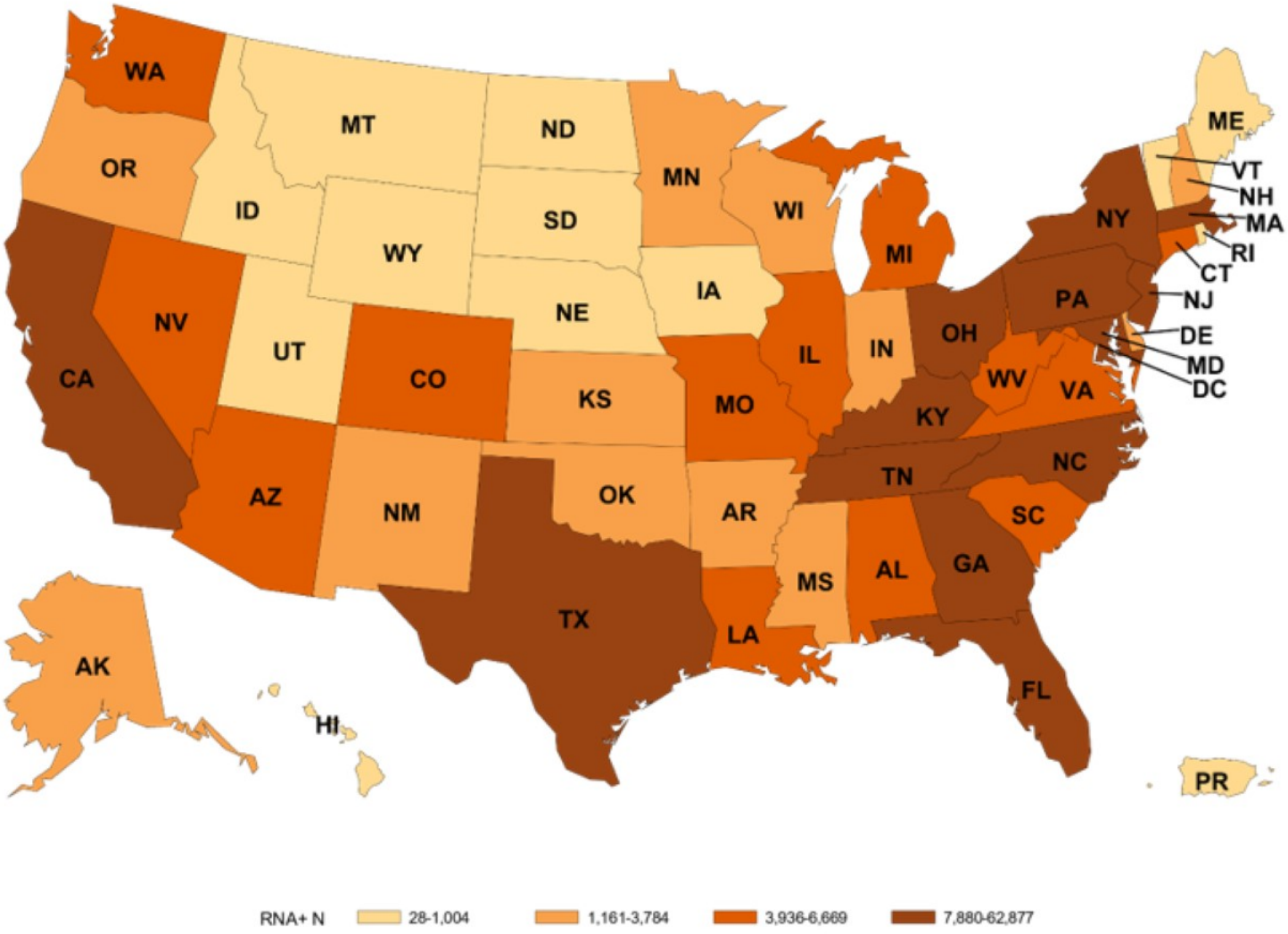
ORIGINAL PAPER

Barriers to Hepatitis C Screening in a Minority Population: A Comparison of Hepatitis C and Human Immunodeficiency Virus Screening Rates at a Community STD Clinic in Miami, Florida

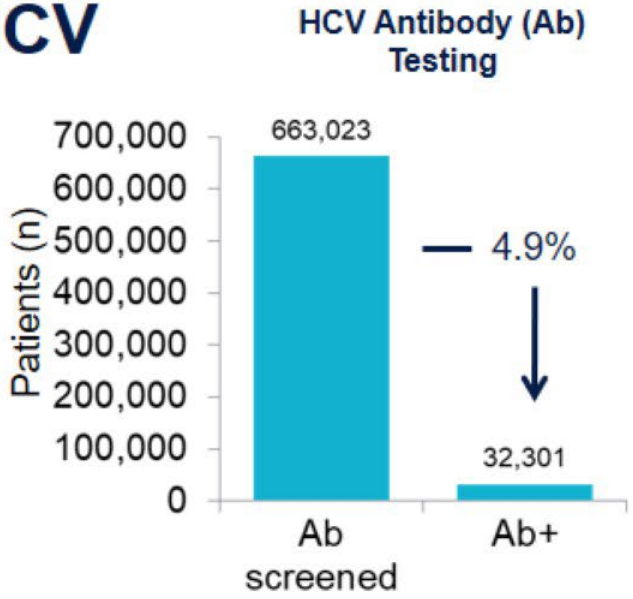
Erica B. Feldman[1] · Raymond Balise[1] · Eugene Schiff[1] · Nicole Whitehead[2] · Emmanuel Thomas[1,3]

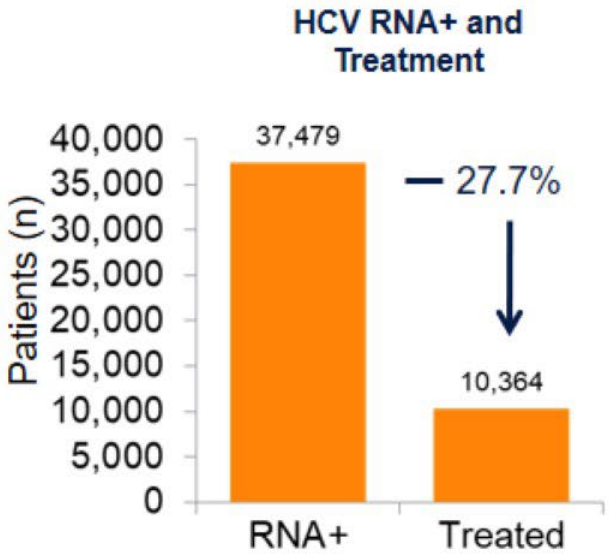
Published online: 28 March 2017

USA: 2016 HCV RNA+ Count



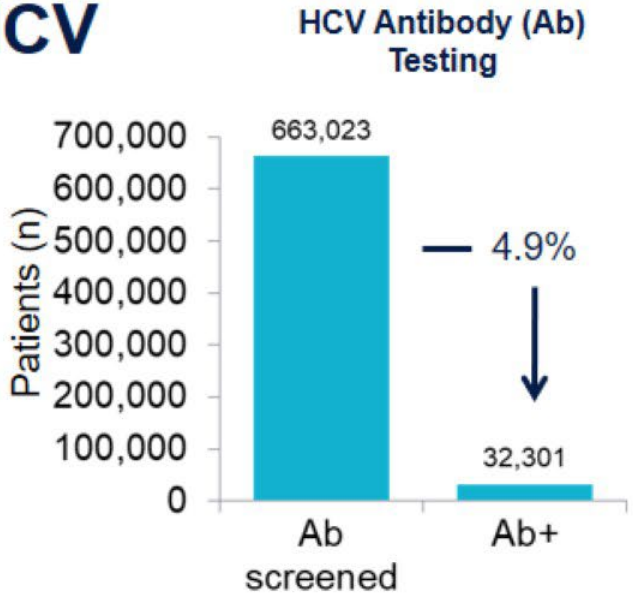
Florida 2016 HCV

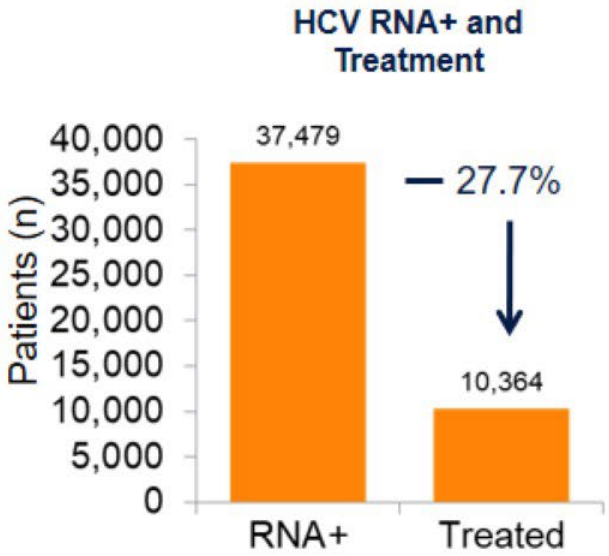




https://mappinghepc.com

Florida 2016 HCV



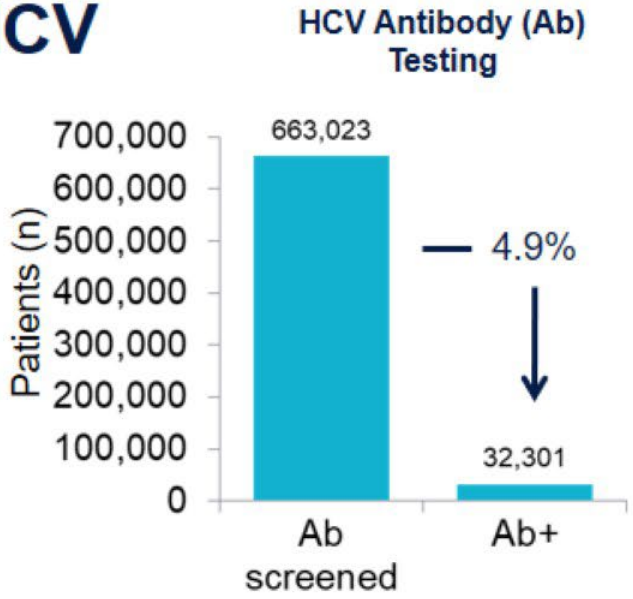


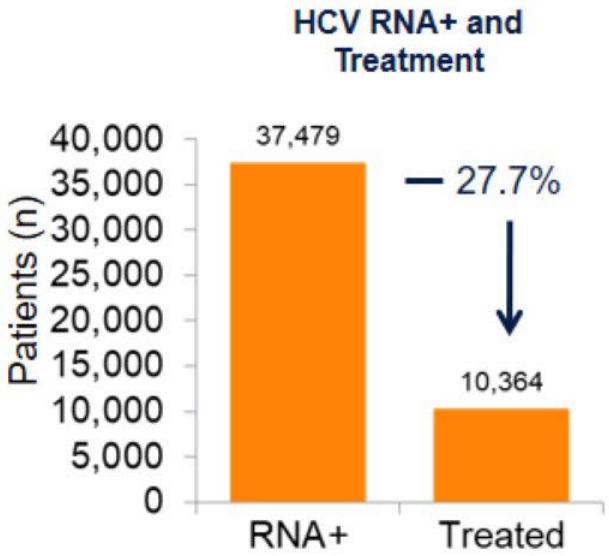
https://mappinghepc.com

Louisiana has a goal of treating more than 10,000 Medicaid-enrolled and incarcerated individuals by the end of 2020.

Florida 2016 HCV

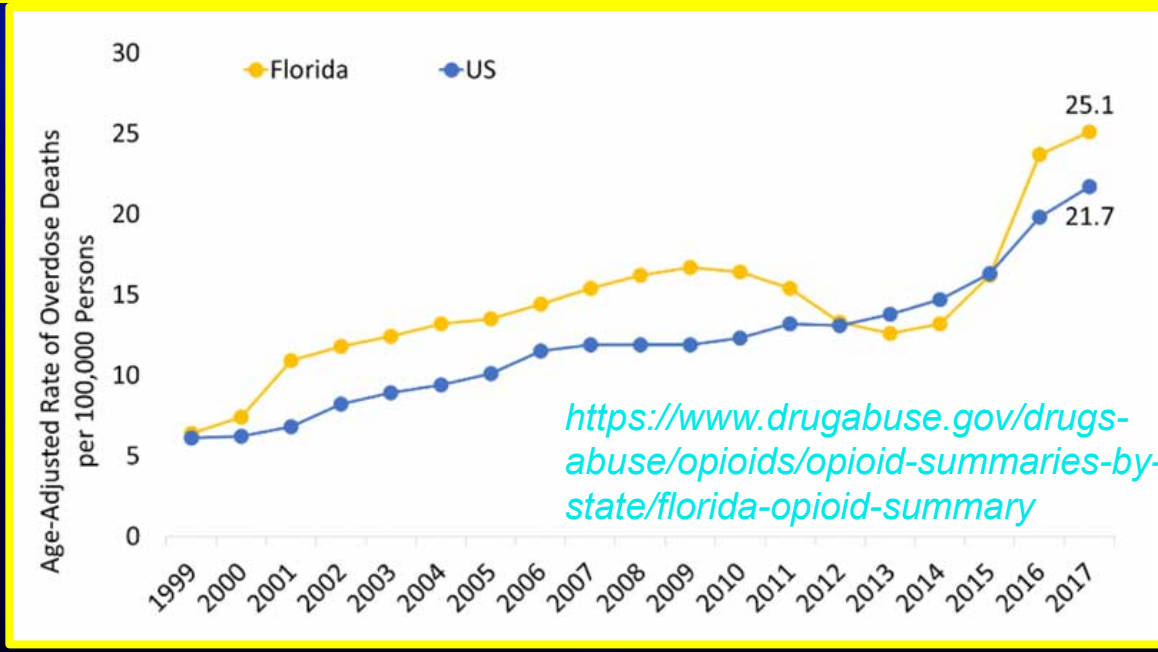
https://mappinghepc.com



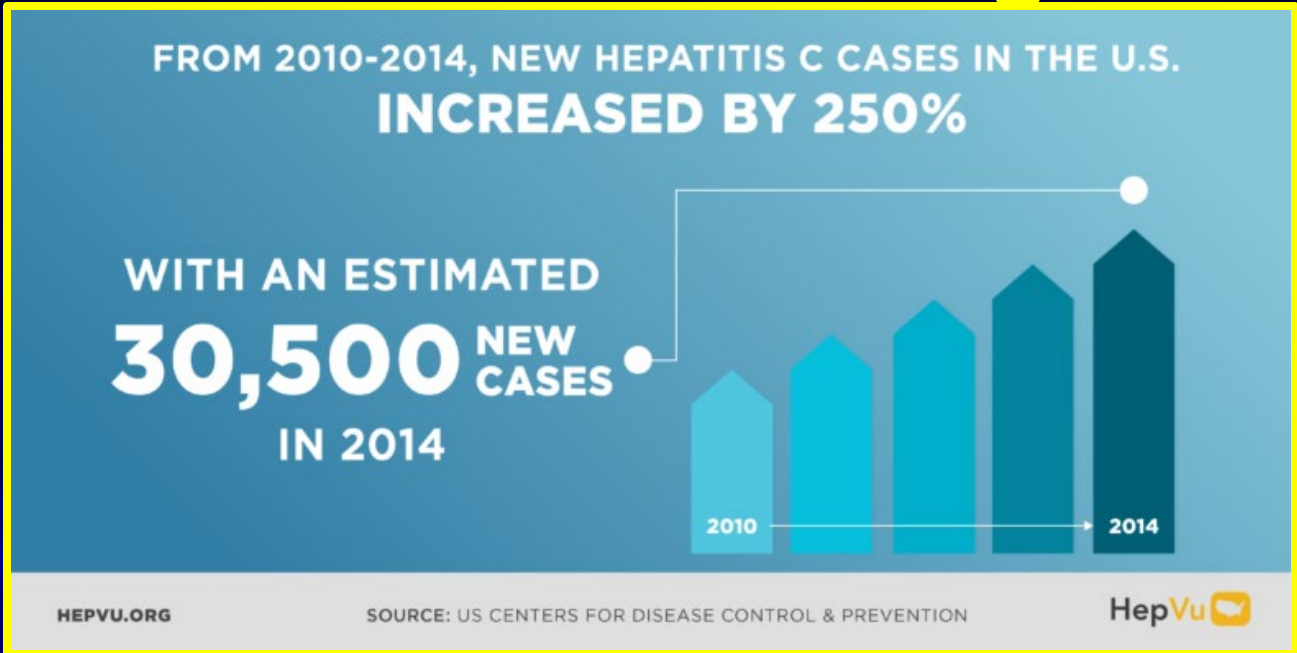


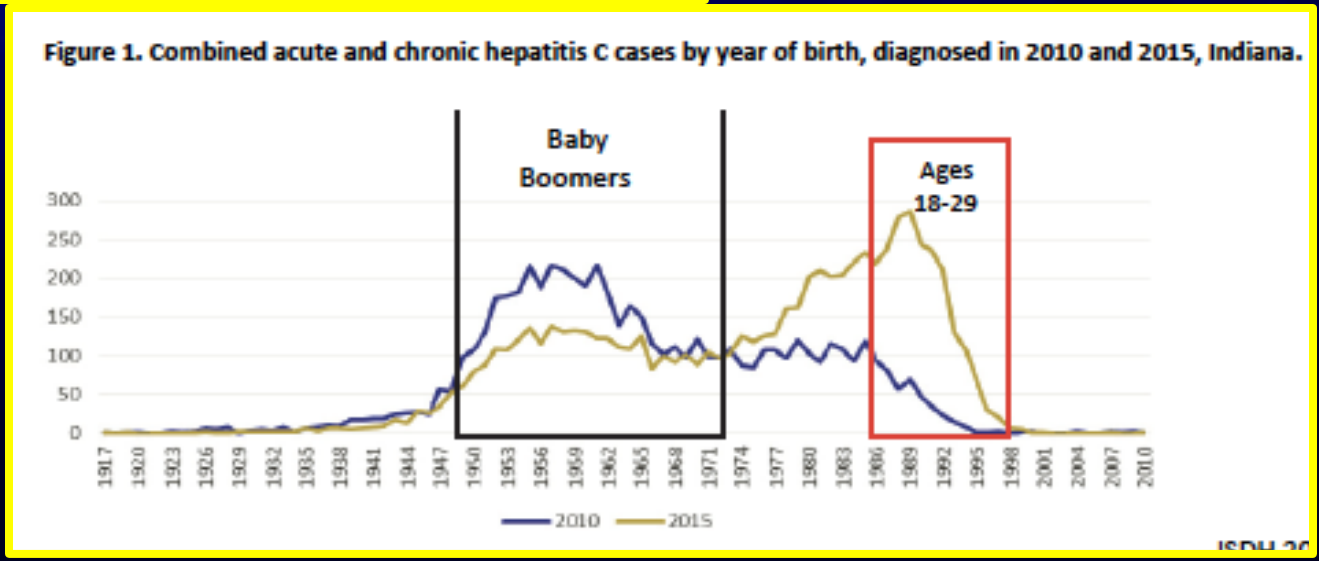
Treatment as Prevention for HCV in FL Does Not Appear to be Working.

- -Complacency
- -Reinfection
- -Not 100% cure rate
- -FL specific Tx barriers
- -Can't treat our way out of this…need SSPs/MAT



HCV Infection Rising in Young Adults

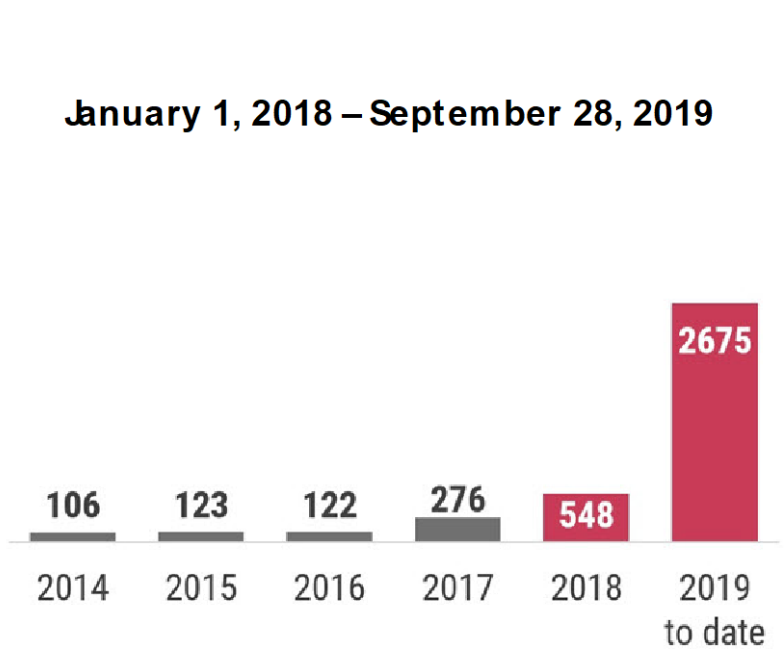




Hepatitis A in FL-A Drain on Limited Resources

Hepatitis A in Florida

From January 1, 2018 through September 21, 2019, **3,223** hepatitis A cases were reported.



The number of reported hepatitis A cases more than doubled from 2016 to 2017 and nearly doubled again in 2018 after remaining relatively stable in previous years. Case counts in 2019 have already surpassed those in 2018.

Florida Surgeon General Scott A. Rivkees Issues Public Health Emergency in Response to Hepatitis A Outbreak

August 01, 2019

Opioid & Health Indicators
Florida

HIV

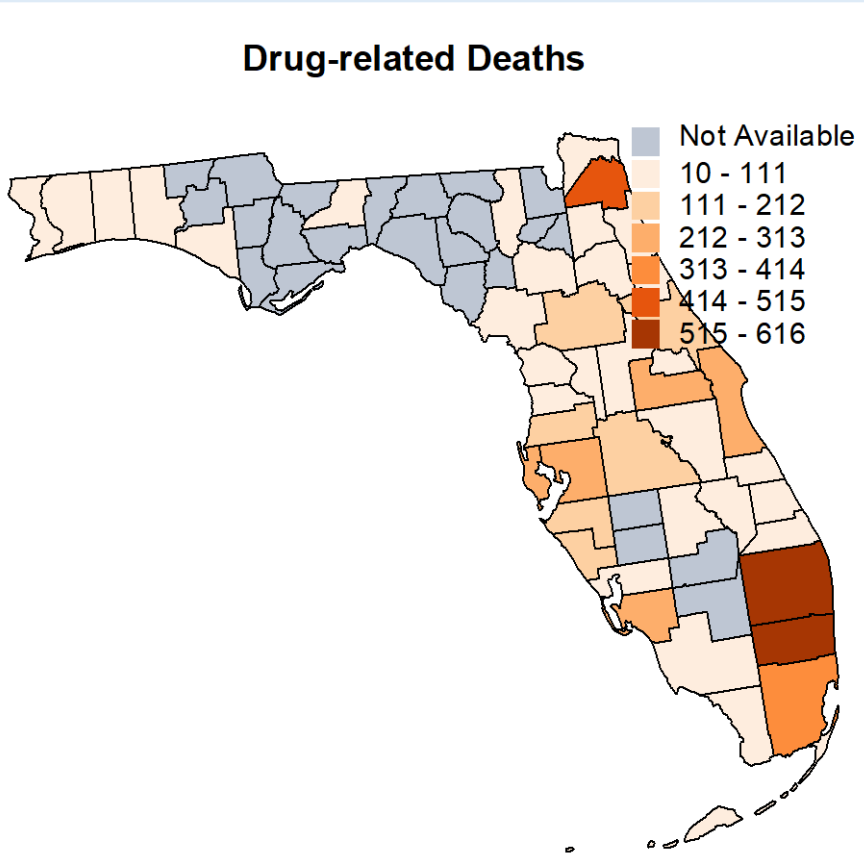
Number of People Living with Diagnosed HIV		U.S.
	108,003	989,222
HIV Prevalence per 100,000		
State Rank: 49	610.8	365.5

Hepatitis C (HCV)

Number of People with Hepatitis C		U.S.
	151,000	2,266,700
Estimated Acute Hepatitis C Cases per 100,000		
State Rank: 37	15.29	13.9

Drug-related Deaths

Drug-related Deaths		U.S.
	5,088	70,237
Drug-related Deaths per 100,000		
State Rank: 36	24.2	21.56



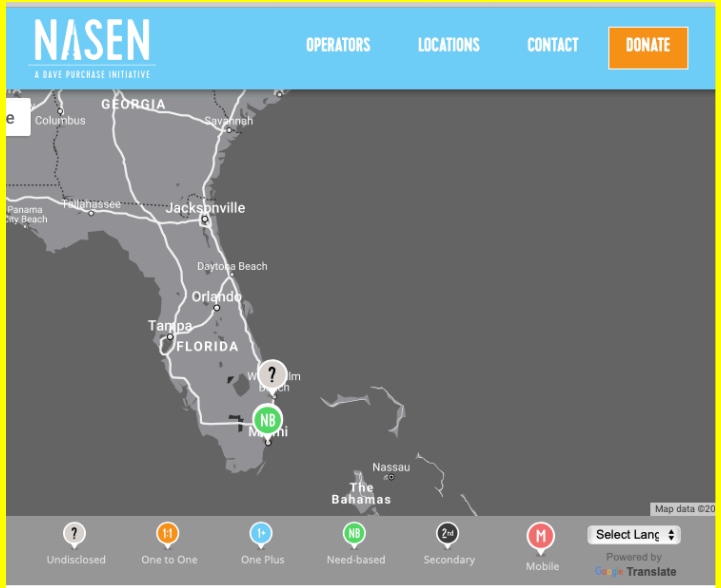
https://opioid.amfar.org/FL

Florida Academic Cancer Center Alliance
Hepatitis C Virus Elimination Meeting

Morning Agenda

9:15-10:00am	**Funding opportunities: PCORI PaCR, NIH Promoting Evidence-Based Screening** Group discussion
10:00-10:30am	**Next steps** Group discussion
10:30-10:45am	**Break**
10:45-11:00am	**Welcome with stakeholders** David Nelson
11:00-11:15am	**Overview of HCV elimination efforts in Florida** Emmanuel Thomas
11:15-12:15pm	**HCV screening portfolio** University of Florida, University of Miami, Moffitt Cancer Center
12:15am-1:15pm	**Lunch** Boxed lunches available in the lobby

Florida-
Syringe Services Program



SEP Locations

Please be aware that this directory includes only those SEPs that are either NASEN Buyers Club Members and have given NASEN authorization to publish their agencies information on this directory or have authorized Buyers Club to publish their information solely for NASEN directory purposes. It is not, nor is it intended to be, a comprehensive listing of all SEPs in the US.

If you operate an SEP and would like to be included in this directory or would like to update your agencies information please reach out to Stephanie@nasen.org

If you operate an SEP and would like to be included in this directory please fill out a Buyers Club Application. Please mark "yes" to the question, "May we publish your information in the NASEN map/directory".

Please be aware if your agency does not respond to annual NASEN directory updates within 30 days your agency may be removed and listed as inactive.

Showing **3** SEPs | State: Florida (3 SEPs) | SEP Type: Undisclosed (175 SEF | Filter

EXCHANGE	ORGANIZATION	CITY	STATE
Flashlight of Hope Inc	Flashlight of Hope Inc.	Miami	FL
IDEA Exchange	Miami IDEA Exchange-Florida Needle Exchange	Miami	FL
Rebel Recovery FL	Rebel Recovery FL	West Palm Beach	FL

The opioid crisis is fueling a dramatic increase in infectious diseases associated with injection drug use.

Reports of acute hepatitis C virus (HCV) cases rose 3.5-fold from 2010 to 2016.[1]

The majority of new HCV infections are due to injection drug use.

Over 2,500 new HIV infections occur each year among people who inject drugs (PWID).[2]

Syringe Services Programs (SSPs) reduce HIV and HCV infections and are an effective component of comprehensive community-based prevention and intervention programs that provide additional services. These include vaccination, testing, linkage to infectious disease care and substance use treatment, and access to and disposal of syringes and injection equipment.

Miami IDEA SSP Numbers

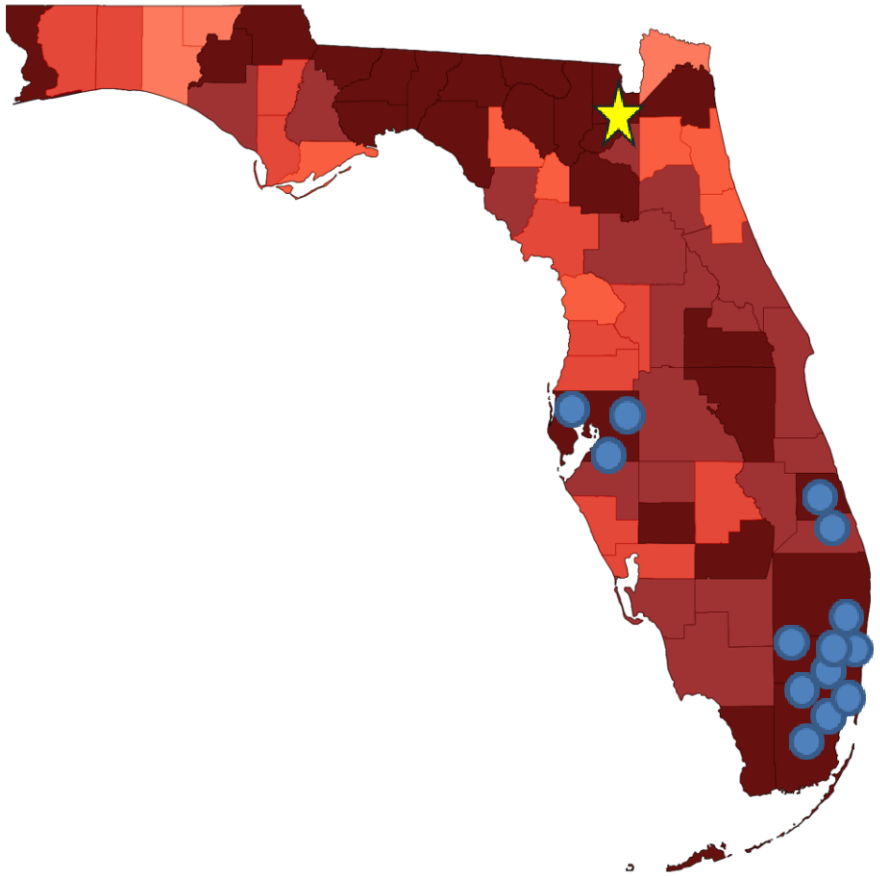
New HCV Diagnosis	Total (N)=112
HCV RNA Positive Chronic	77
HCV RNA Positive Acute	2
HCV RNA Positive/HIV Positive	8
HCV RNA Negative	25

Iyengar *et al. Harm Reduction Journal* (2019) 16:7

Florida Partner Reach in 2019

Current FOCUS Partners

1. **Care Resource**
2. **Baptist Health South Florida:** ***Homestead Hospital and West Kendall Baptist Hospital***
3. **Tampa General Hospital:** ***TGH ED & Brandon HealthPlex***
4. **Metro Inclusive Health**
5. **Genesis Community Health**
6. **Jackson Health Systems: Jackson Memorial Hospital, Jackson South & Jackson North**
7. **FoundCare**
8. **Memorial Regional Hospital**
9. **University of Miami's IDEA Exchange**
10. **University of Miami Health ED**
11. **University of Florida Health ED Jacksonville***



Rates of Persons Living with an HIV Diagnosis
County, Florida, 2015

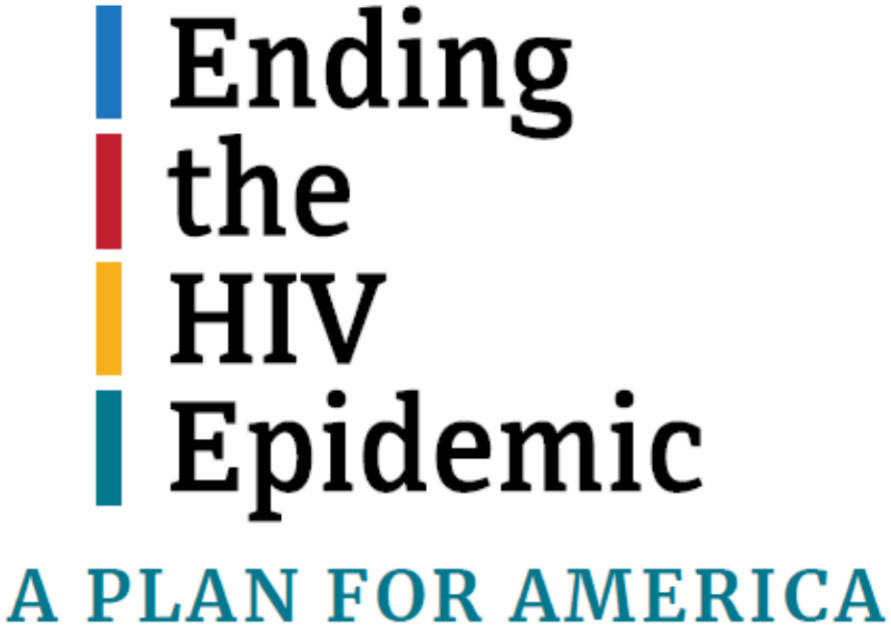
AIDSVu

0 - 50	51 - 60	61 - 80	81 - 90	91 - 120	121 - 150	151 - 190	191 - 250	251 - 380	381+

* Data not shown to protect privacy because of a small number of cases and/or a small population.
** State health department, per its HIV data re-release agreement with CDC, requested not to release data to AIDSVu.
NOTE: There are no counties in Alaska, the District of Columbia and Puerto Rico.

Florida Counties

FL had the highest number of newly diagnosed cases in 2016, concentrated in seven counties



- **Broward County**
- **Duval County**
- **Hillsborough County**
- **Miami-Dade County**
- **Orange County**
- **Palm Beach County**
- **Pinellas County**

Source: www.HIV.gov/ending-hiv-epidemic

Florida Counties

Ending the HIV Epidemic – A Plan for America

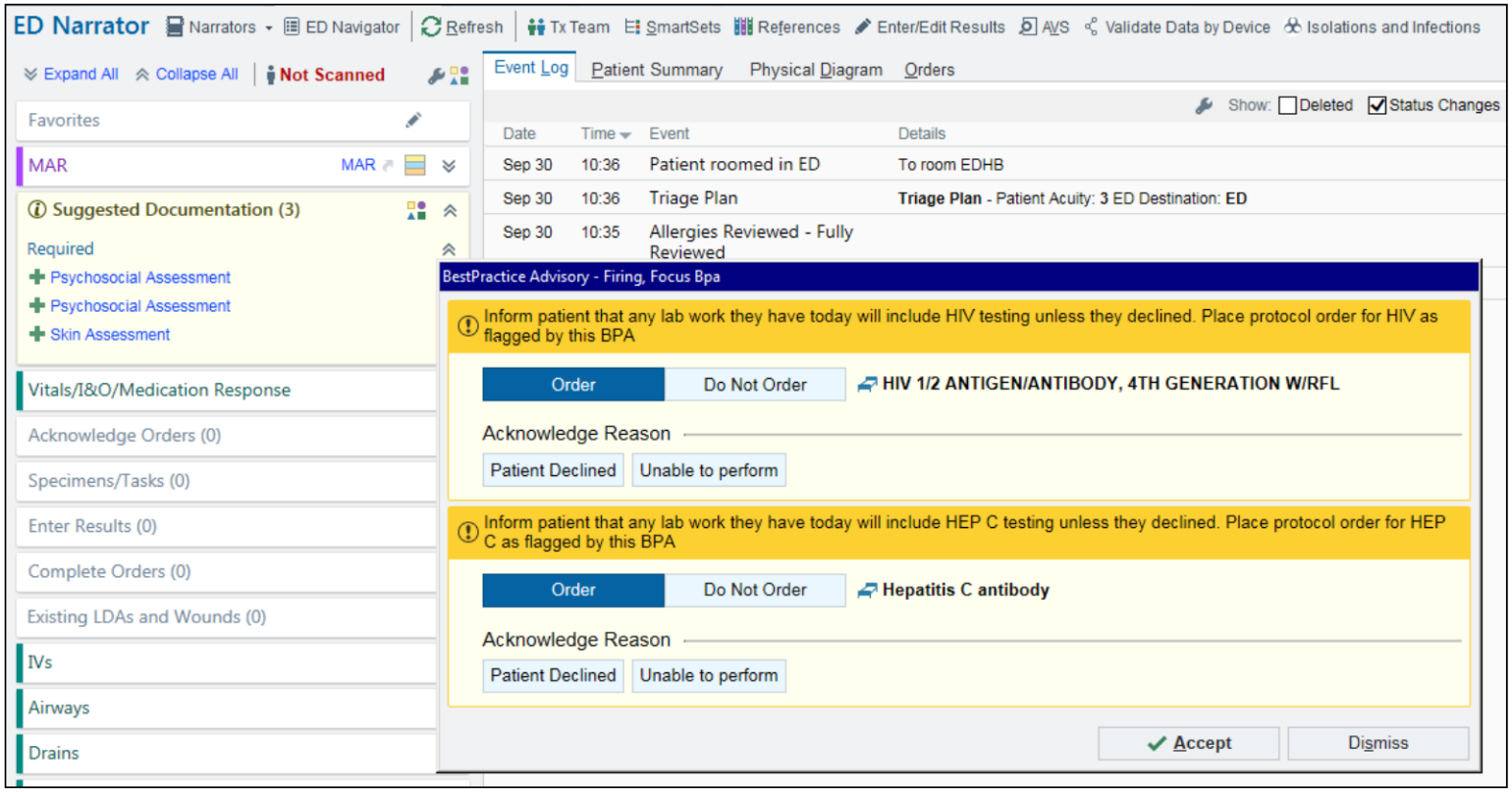
- **Miami-Dade County**
  - M-DC DoH
  - Baptist Health
  - Jackson Health System
  - University of Miami
    - IDEA Exchange
    - UHealth ED
- **Broward County**
  - Broward County DoH
  - Memorial Health System
- **Palm Beach County**
  - Palm Beach County DoH
- **Orange County**
  - Orange County DoH / Dr. Beal
- **Hillsborough County**
  - Hillsborough County DoH
  - Tampa General Hospital
  - Metro Inclusive Health
- **Pinellas County**
  - Pinellas County DoH
  - Metro Inclusive Health
- **Duval County**
  - Duval County DoH
  - UF Health in Jacksonville

Gilead FOCUS Program

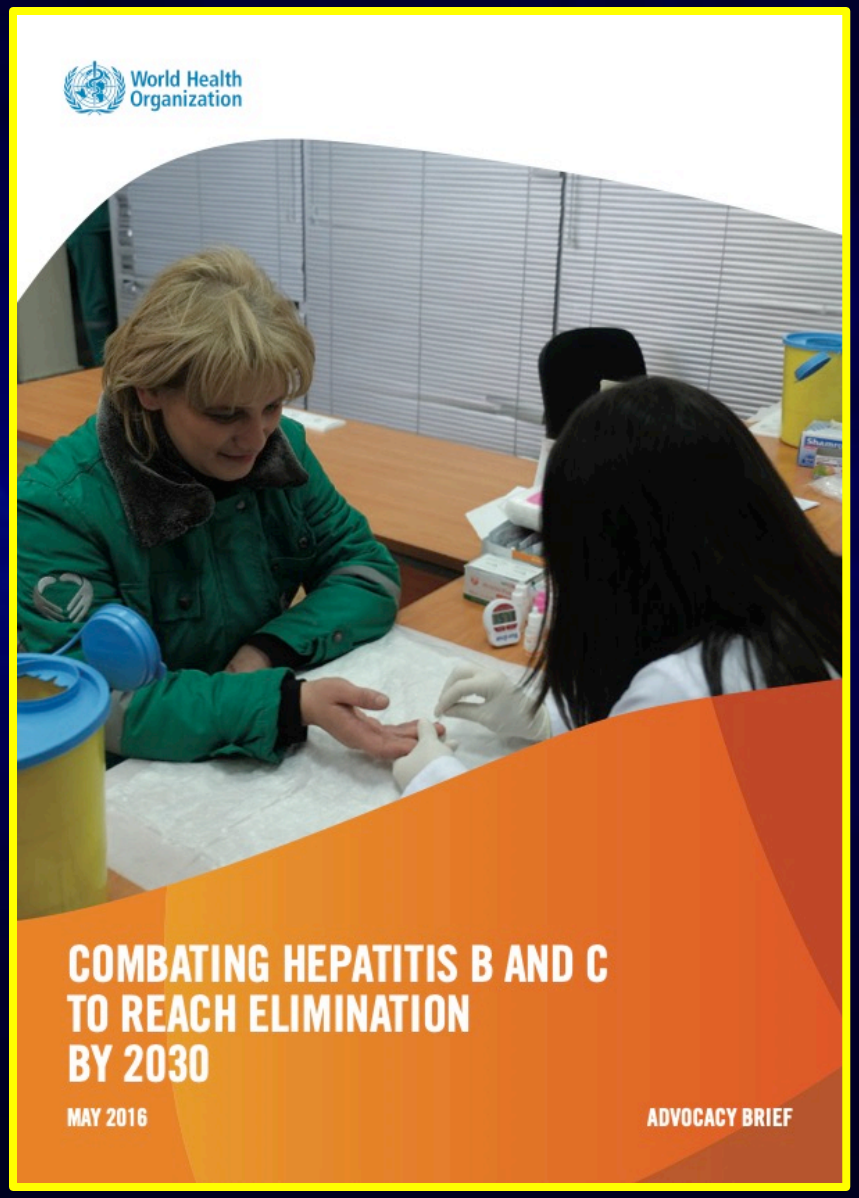
- 1/1/19 $300,000 per year
- Will Screen approximately 10,000 patients
- Grant supports complete screening infrastructure and linkage to care
- Funding available for subsequent years
- Expand program to screen for HBV
- Data obtained can be leveraged for future grants that will impact our community

Effective Wednesday, October 9, a new **Best Practice Advisory (BPA) for HIV/HEP screening** will be available in the Emergency Department at UTower. This BPA will help identify the undiagnosed and facilitate a seamless path to medical care.

The BPA will appear once the nurse opens the patient's chart within the **ED Narrator**.



HCV Elimination Program



HCV Elimination Program

- AASLD meeting in Miami 2/1/2019
- Predict USA achieving WHO goals >2050
- Opioid epidemic (new wave of HCV infec.)
- Lack of an HCV vaccine
- Reinfection
- Currently 8 week treatment regimen
- Lack of ideal POC tests for infection (T&T)
- Less than 100% cure rates
- Cost of Medications

Conference Reports for NATAP

2019 AASLD/EASL HCV
Special Conference 01-02
February 2019, Miami, FL

Back

Global timing of hepatitis C virus elimination: estimating the year countries w the World Health Organization elimination targets

Reported by Jules Levin

2019 AASLD/EASL HCV Special Conference 01-02 February 2019, Miami, FL

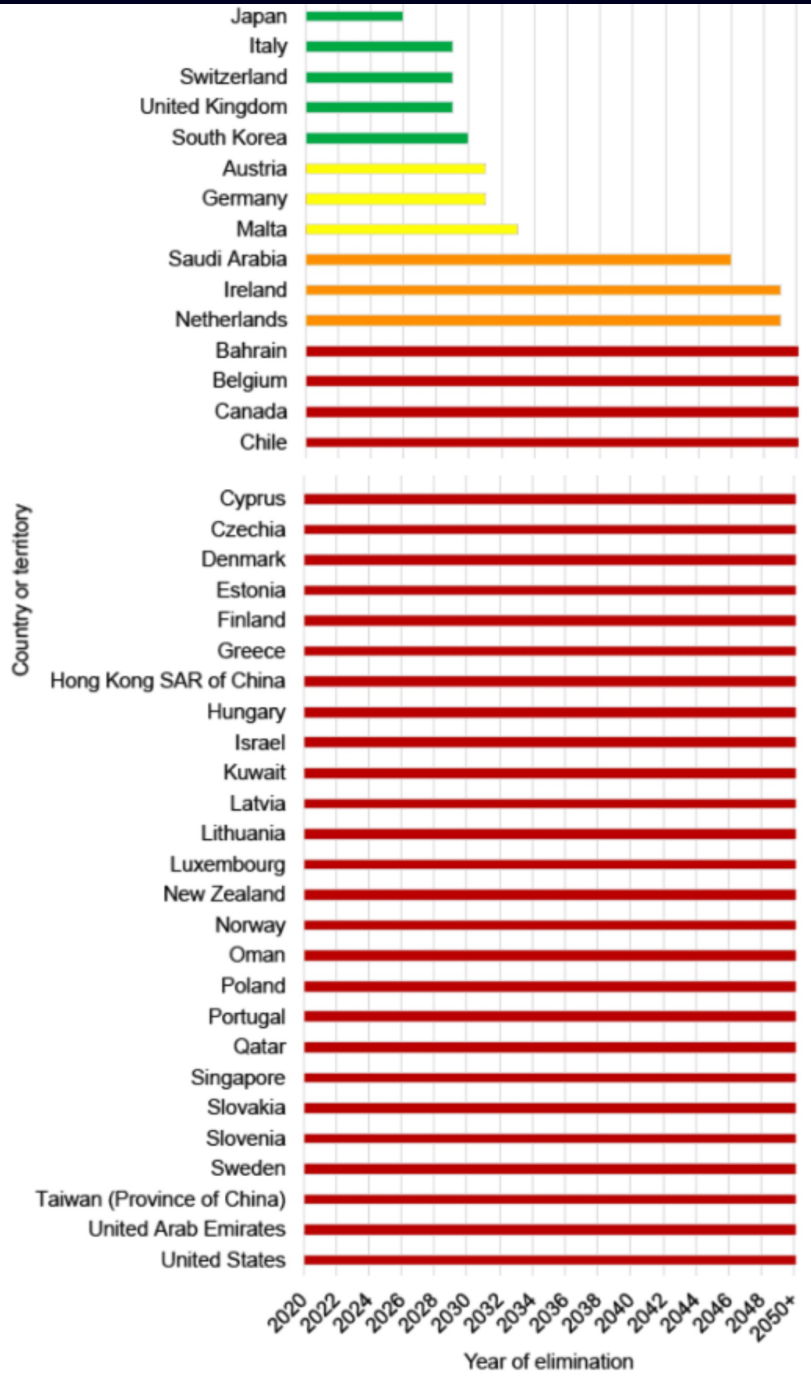
Homie Razavia, Yuri Sanchez Gonzalezb, Andreas Pangerlb, Markus Cornbergc a Center for Disease A Lafayette, CO, United States, b AbbVie Inc., North Chicago, IL, United States, c Department of Gastr Hepatology and Endocrinology, Medizinische Hochschule Hannover, Hannover, Germany

Conclusions

Despite the introduction of curative therapies, 80% of high-income countries and territories ar on track to meet the WHO's targets that would eliminate HCV as a public health threat by 203 while 67% are off-track by at least 20 years. Immediate action to improve HCV diagnosis and treatment is needed to make the global elimination of HCV by 2030 an attainable goal.

Background

- The introduction of highly efficacious pan-genotypic therapies for hepatitis C virus (HCV) infe has made the elimination of HCV an attainable goal
- This study assessed the progress made in 45 high-income countries and territories towards meeting the 2030 HCV elimination targets by the World Health Organization (WHO) for incid mortality, diagnosis, and treatment



HCV — hepatitis C virus; Hong Kong SAR of China — Hong Kong Special

Curing HCV-Infected Uninsured Patients Treatment Cascade

DeBose-Scarlett *et al. J Transl Med (2018) 16:178*
https://doi.org/10.1186/s12967-018-1555-y

Journal of Translational Medicine

RESEARCH Open Access

Obstacles to successful treatment of hepatitis C in uninsured patients from a minority population

Alexandra DeBose-Scarlett[1], Raymond Balise[1,5], Deukwoo Kwon[1,5], Susan Vadaparampil[2], Steven Xi Chen[1,5], Eugene R. Schiff[3,5], Gladys Patricia Ayala[4] and Emmanuel Thomas[1,3,5,6*]

Abstract

Background: Hepatitis C virus (HCV) treatment regimens (DAAs) are well tolerated, efficacious but costly. Their high cost and restricted availability, raises concerns about the outcome of treatment in uninsured patients. This study investigated sustained virologic response (SVR) outcomes in a predominately uninsured patient population and completion of four steps along the HCV treatment cascade.

Methods: A retrospective chart review was conducted to characterize the patient population and analyze covariates to determine association with insurance status, attainment of SVR and progression through the HCV treatment cascade.

Results: Out of a total of 216 patients, 154 (71%) were uninsured. Approximately 50% of patients (109 of 216 patients) were male and 57% were Hispanic (123 of 216 patients). Sex, race, ethnicity, treatment compliance, and rates of complications were not associated with insurance status. Insured patients were older (median 60 years vs 57 years, p-value < 0.001) and had higher rates of cirrhosis: 32 out of 62 patients (52%) vs 48 out of 154 patients (31%) (p-value = 0.005). Insured patients were tested for SVR at similar rates as uninsured patients: 84% (52 of 62 patients) vs 81% (125 of 154 patients), respectively. Of those tested for SVR, the cure rate for insured patients was 98% (51 out of 52 patients) compared to 97% (121 out of 125 patients) in the uninsured. Out of those who completed treatment, 177 of 189 (94%) were tested for attainment of SVR. Compliance rates were significantly different between tested and untested patients: 88% (156 of 177 patients) vs 0% (0 of 12 patients), respectively (p-value < 0.001). However, insurance status, race ethnicity, cirrhosis, and complications were not associated with being tested for SVR.

Conclusions: These results demonstrate that insured and uninsured patients with chronic HCV infection, with access to patient assistance programs, can be treated and have comparable clinical outcomes. In addition, testing for SVR remains an important obstacle in completion of the HCV treatment cascade. Nevertheless, patient assistance programs remove a significant barrier for treatment access in real-world HCV infected populations.

Keywords: Hepatitis C virus, Sustained virologic response, Direct acting antivirals, Uninsured, Minority

Background

Hepatitis C virus (HCV) is a significant global health problem [1, 2]. An estimated 130–180 million individuals are currently infected [3], with 3–4 million new infections each year [3]. An estimated 2.7–3.9 million people in the United States currently live with HCV and 15,000 die each year due to HCV disease and resultant hepatic complications [4]. However, these numbers are likely an underestimation of the true disease burden because the highest risk groups are often under-represented in general population studies [5].

Approximately 85% of infections progress to chronicity [3]. Chronic infection can lead to cirrhosis, hepatocellular

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Full list of author information is available at the end of the article

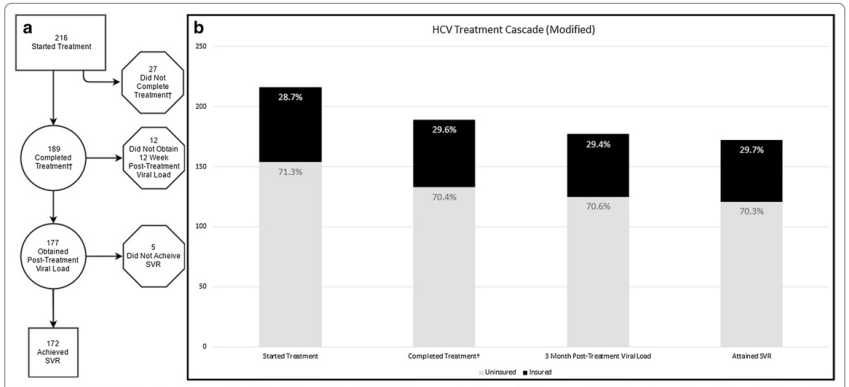
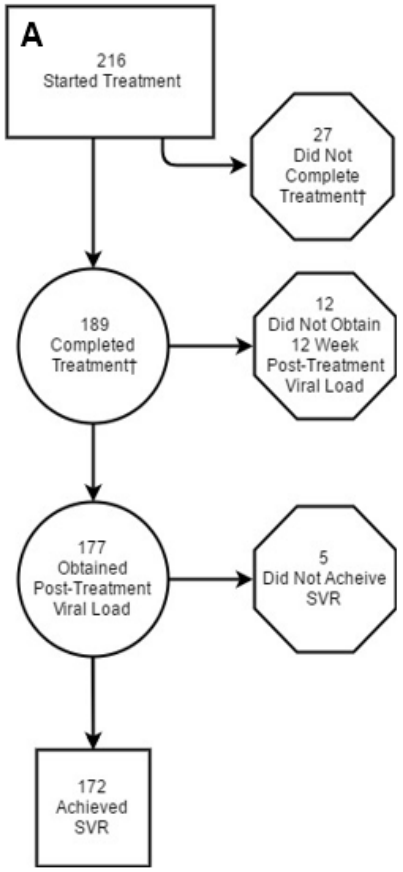
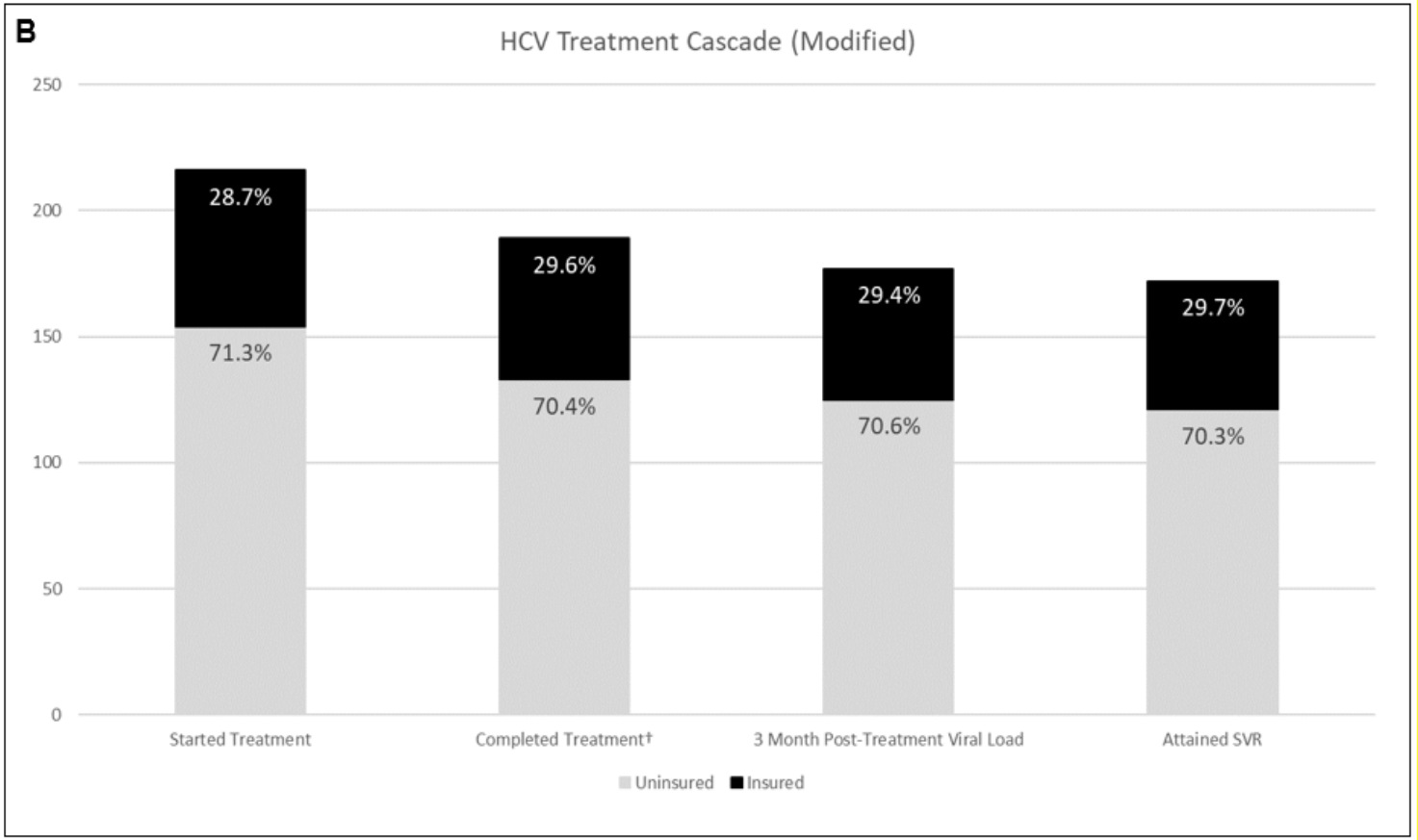


Fig. 1 Modified HCV treatment cascade. **a** Absolute counts of patients progressing through the cascade. **b** Percentage of insured and uninsured patients at each step. †Completed treatment per guidelines (based on patient report)

HCV Treatment Outcomes





FL DOH Funding

- 5-year $2M Clinical Cancer Research Award
- Identify Covariates for HCC Development

-South Florida cohort of patients with liver disease at risk to develop HCC

-Cross-sectional study of existing data

-Prospective, longitudinal study incorporating yearly Fibroscan

-To understand which patients are most at risk of developing HCC to facilitate early detection.

Non-Invasive Assessment of Fibrosis

- **Initial Cross-sectional study**
- **Utilizes Transient Elastography (Liver Stiffness increases with fibrosis/cirrhosis)**
- Yoneda M, Thomas E, Schiff ER: *Clinical Gastroenterology and Hepatology* 2015

Non-Invasive Assessment of Fibrosis in Obese Patients

- Yoneda M, Thomas E….Schiff ER: *Clinical Gastroenterology and Hepatology* 2015

August 2015

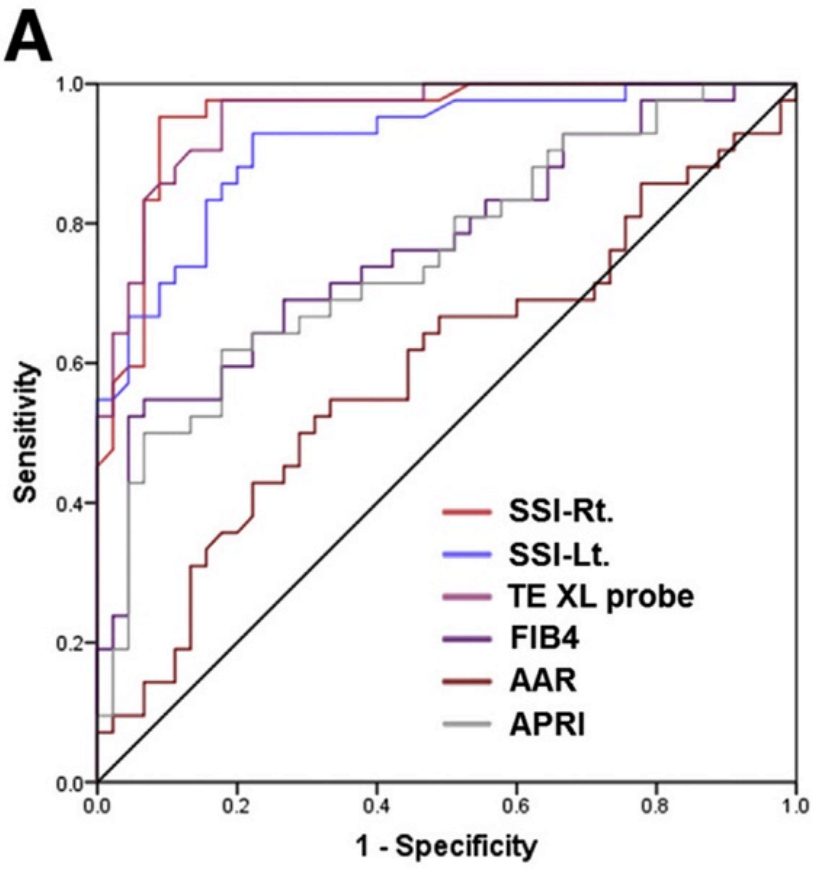


Figure 3. Receiver-operating characteristic curves for detecting (*A*) severe fibrosis (fibrosis stages 3–4) and (*B*) cirrhosis in 124 biopsy-proven patients with liver disease from all etiologies.

Non-Invasive Assessment of Fibrosis

Liver Biopsy	
Metavir (F)	*N*
0	48
1	111
2	104
3	56
4	154
Total	473

Category	F4 Only
No	319
Yes	154

UVA			
Covariate	*OR*	*p-value*	*AUC*
age	1.03	0.0173	0.568
bmi	1.05	0.0523	0.56
ast	1.01	<.0001	0.625
alt	1	0.3503	0.514
platelets	0.98	<.0001	0.827
albumin	0.06	<.0001	0.788
fib4 index	2.11	<.0001	0.833
fibroscan	1.23	<.0001	0.925

MVA1			
Covariate	*OR*	*p-value*	*AUC*
age	1.01	0.5045	0.94
bmi	1.01	0.8708	
ast	1	0.9797	
platelets	0.983	0.0003	
albumin	0.21	0.0019	
fib4 index	1.01	0.966	
fibroscan	1.15	<.0001	

MVA2			
Covariate	*OR*	*p-value*	*AUC*
			0.94
platelets	0.98	<.0001	
albumin	0.19	0.0005	
fibroscan	1.15	<.0001	

Category	F3 & F4
No	263
Yes	210

UVA			
Covariate	*OR*	*p-value*	*AUC*
age	1.02	0.0578	0.554
bmi	1.06	0.0231	0.557
ast	1.01	<.0001	0.597
alt	1	0.2367	0.508
platelets	0.99	<.0001	0.743
albumin	0.15	<.0001	0.701
fib4 index	1.95	<.0001	0.754
fibroscan	1.28	<.0001	0.884

MVA1			
Covariate	*OR*	*p-value*	*AUC*
age	0.98	0.3009	0.891
bmi	1.01	0.7465	
ast	0.99	0.0768	
platelets	1	0.9694	
albumin	1.11	0.8099	
fib4 index	1.54	0.042	
fibroscan	1.26	<.0001	

MVA2			
Covariate	*OR*	*p-value*	*AUC*
			0.888
platelets	0.995	0.0223	
fibroscan	1.28	<.0001	

Non-Invasive Assessment of Fibrosis

Analysis of Clinical Parameters of Liver Disease Based on Race Data from UM EHR.

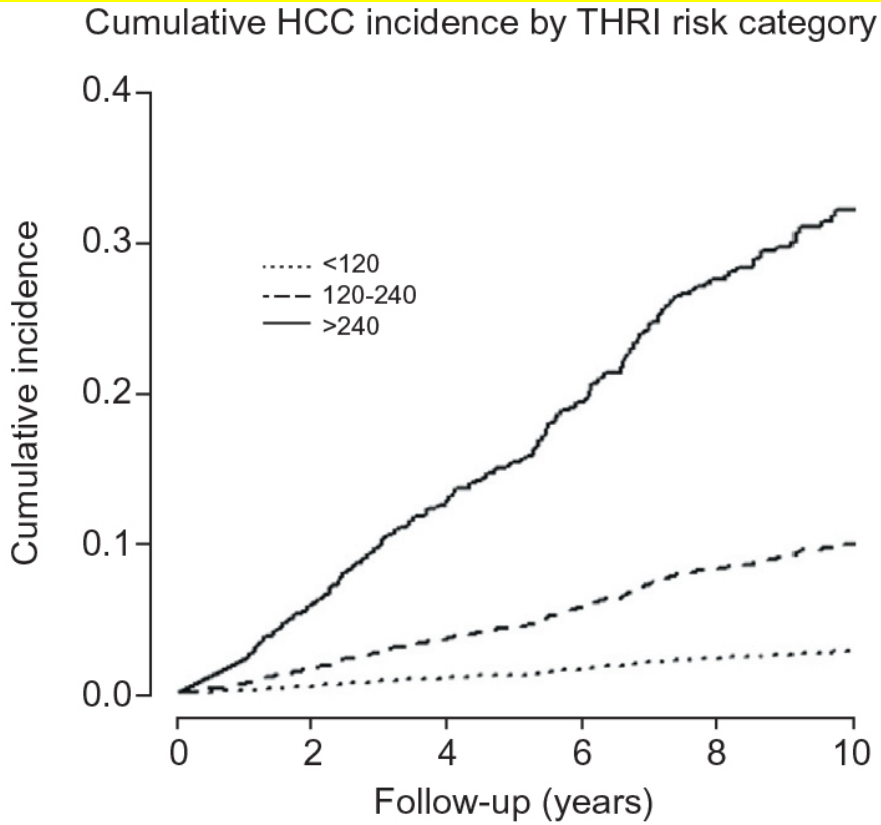
Race	All	Non-Hispanic White	Non-Hispanic Black	Hispanic	Others	Unknown	
Variable	N; Mean±SD	N; Mean±SD	N; Mean±SD	N; Mean±SD	N; Mean±SD	N; Mean±SD	p-value
BMI	995;26.8±4.6	557;26.6±4.5	130;27.8±5.2	229;27.1±4.7	23;23.5±2.8	56;26.1±4.3	0.0001
AST	1169;54.5±66.6	642;55.3±51.9	151;51.8±71.4	284;56.7±94.8	29;43.8±38.5	63;47.5±38.7	0.1723
ALT	1171;63.1±70.1	643;66.5±68.2	151;55.3±90.4	284;62.0±66.9	29;52.8±51.3	64;57.7±51.6	0.0194
Platelets (10^9/L)	1171;193.1±73.2	643;192.4±72.6	151;192.6±70.7	283;194.0±75.9	29;206.3±78.8	65;191.3±72.0	0.7921
Albumin (g/dl)	1158;4.3±1.4	636;4.4±1.9	151;4.2±0.5	281;4.3±0.5	28;4.4±0.3	62;4.3±0.4	0.0136
FIB4 Index	985;2.7±2.8	551;2.7±3.1	130;2.3±1.6	227;2.8±3.0	23;1.9±1.5	54;2.3±1.4	0.2334
Fibroscan (LSM)	1943;11.5±11.6	648;11.9±11.2	149;12.2±12.0	283;12.2±12.4	29;8.3±5.9	834;10.9±11.6	0.0010

Non-Invasive Assessment of Fibrosis HCC Risk Stratification

Components of the Toronto HCC Risk Index.

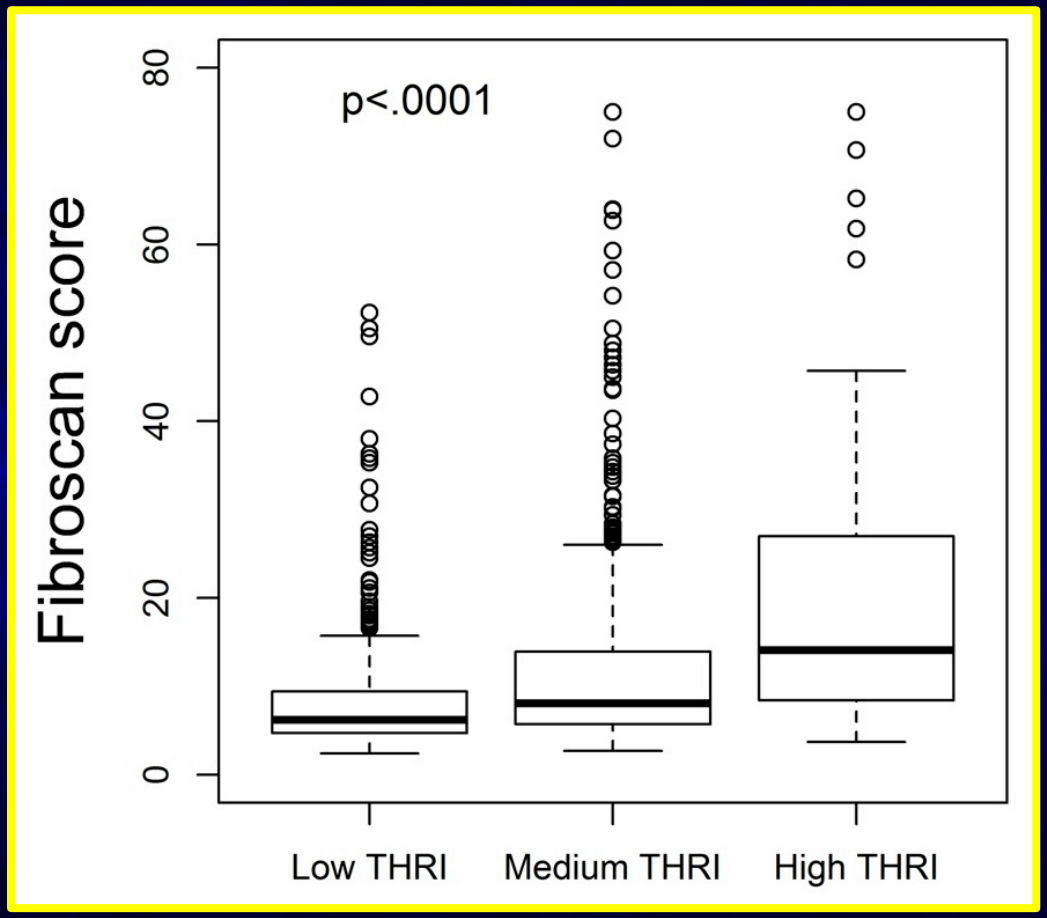
Risk Factor	Score
Age	
<45	0
45–60	50
>60	100
Etiology	
Autoimmune	0
HCV SVR	0
Other	36
Steatohepatitis	54
HCV	97
HBV	97
Gender	
Female	0
Male	80
Platelets	
>200	0
140–200	20
80–139	70
<80	89
Total	0–366

HBV, Hepatitis B virus; HCV, Hepatitis C virus; SVR, sustained virologic response.



Sharma et al., THRI, Journal of Hepatology, August, 2017

Non-Invasive Assessment of Fibrosis HCC Risk Stratification

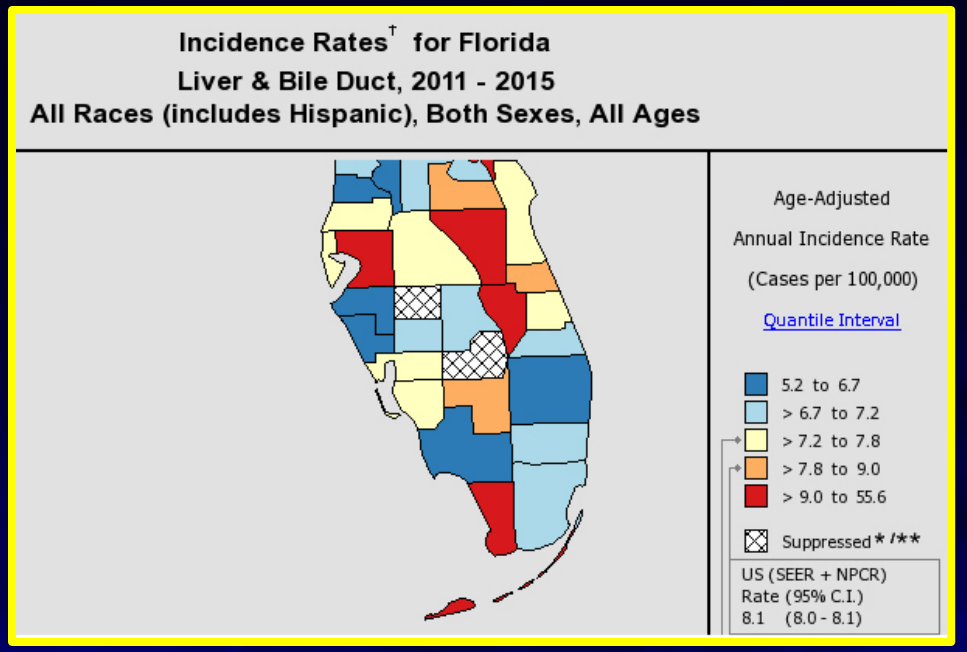


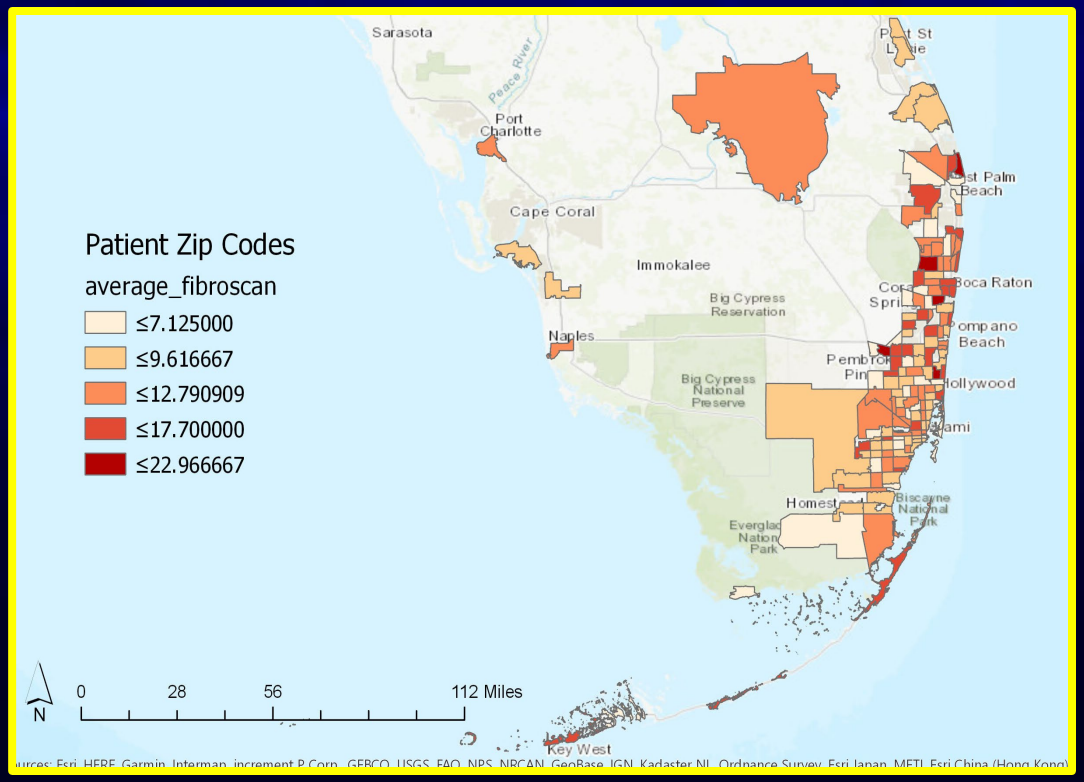
N	UVA F4	OR	p-value	AUC
891	Age	1.048	<.0001	0.647
886	BMI	1.007	0.688	0.523
861	AST	1.008	<.0001	0.635
861	ALT	1.001	0.2649	0.542
891	Patelets	0.981	<.0001	0.808
857	Albumin	0.13	<.0001	0.75
833	Fib4 index	1.445	<.0001	0.818
891	Fibroscan	1.094	<.0001	0.877
886	BMI Cat. (ref: Underwgt/Normal)			
	obese	1.345	0.1221	0.532
891	Scan Cat.(ref: <7)			0.837
	7-11.9	4.187	0.0032	
	12+	46.987	<.0001	
891	THRI (ref: Low)			0.703
	Intermediate	5.567	0.0011	
	High	18.301	<.0001	
844	AST/ALT	2.888	<.0001	0.691
817	APRI	1.769	<.0001	0.761

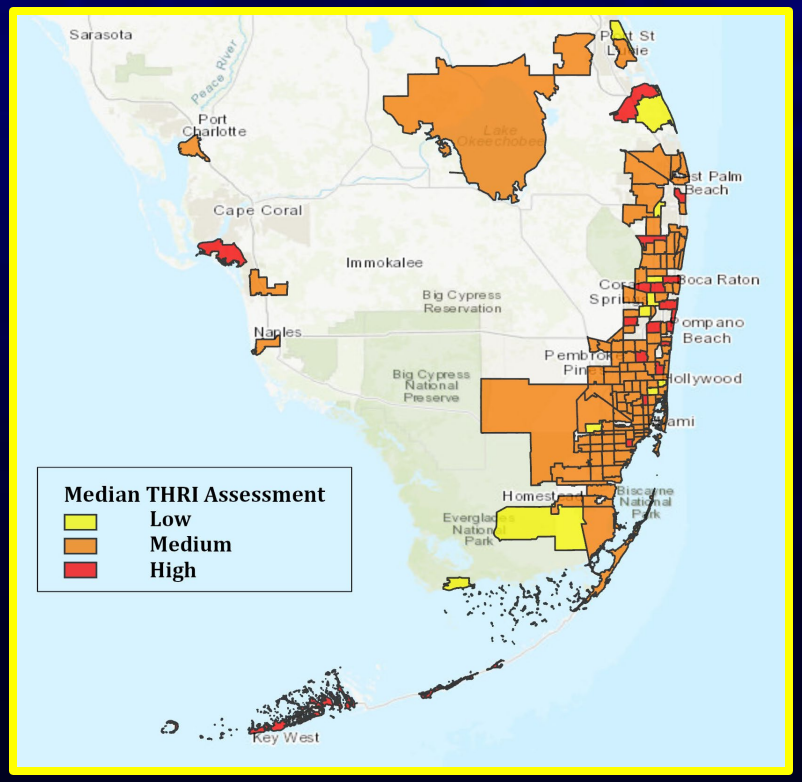
Tatsumi et al., Fibroscan & HCC, Hepatology Research, May, 2015.

Sharma et al., THRI, Journal of Hepatology, August, 2017 (Based on Age, Sex, Liver Disease Etiology, Platelets).

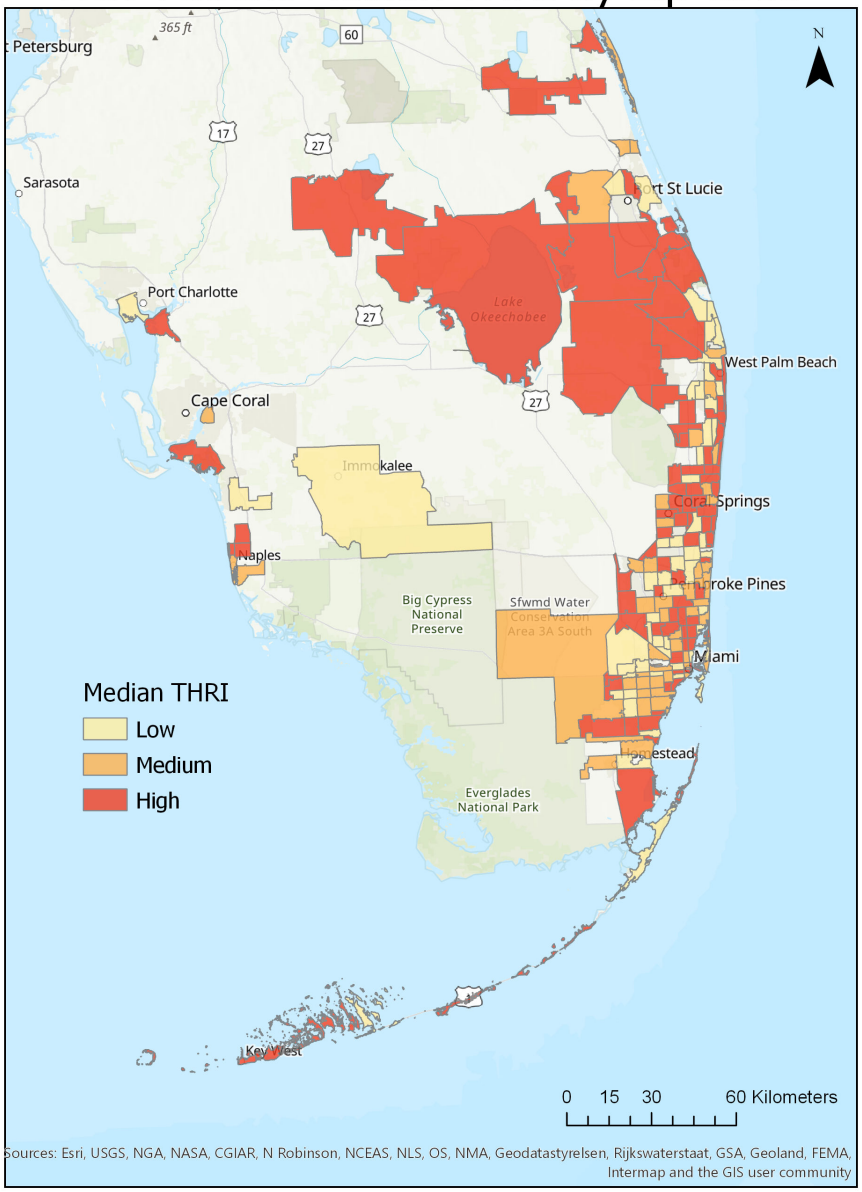
Geographic Assessment of Clinical Parameters





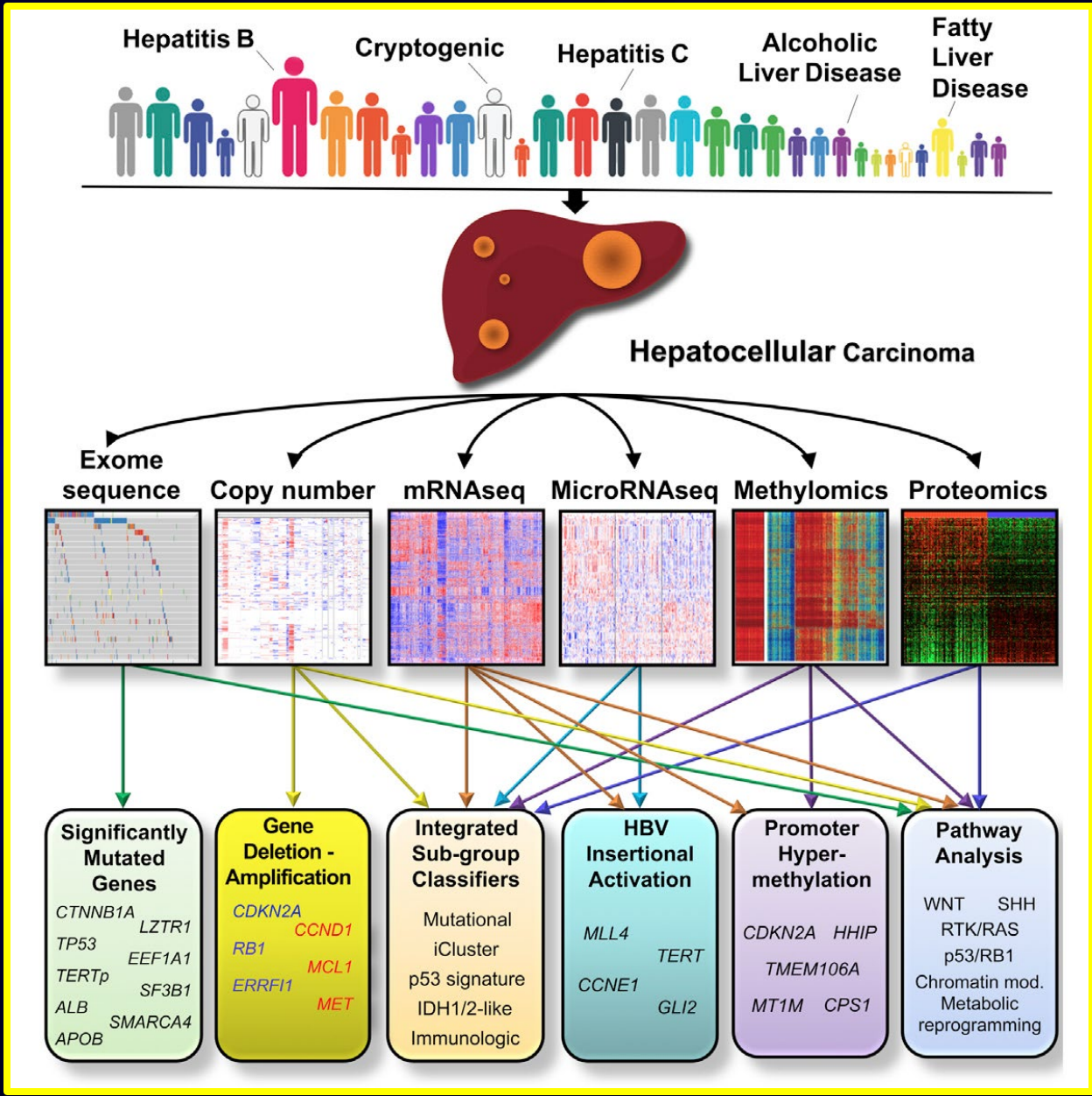


HCV Patient Median THRI by Zip Code



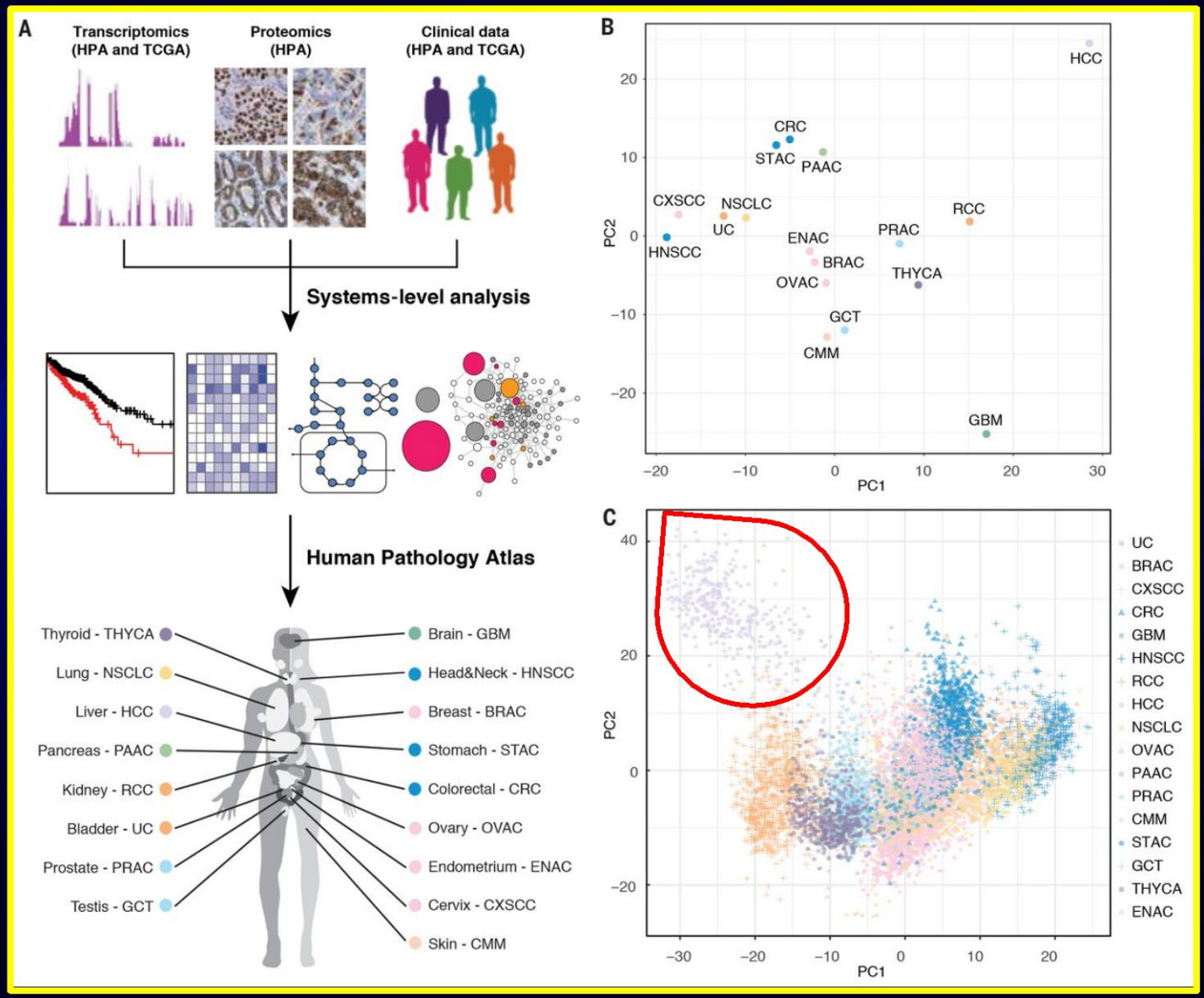
Comprehensive and Integrative Genomic Characterization of Hepatocellular Carcinoma (Somatic Mutations)

77% of HCCs studied had mutations in TERT, p53, & WNT
Driver Mutations Not Druggable



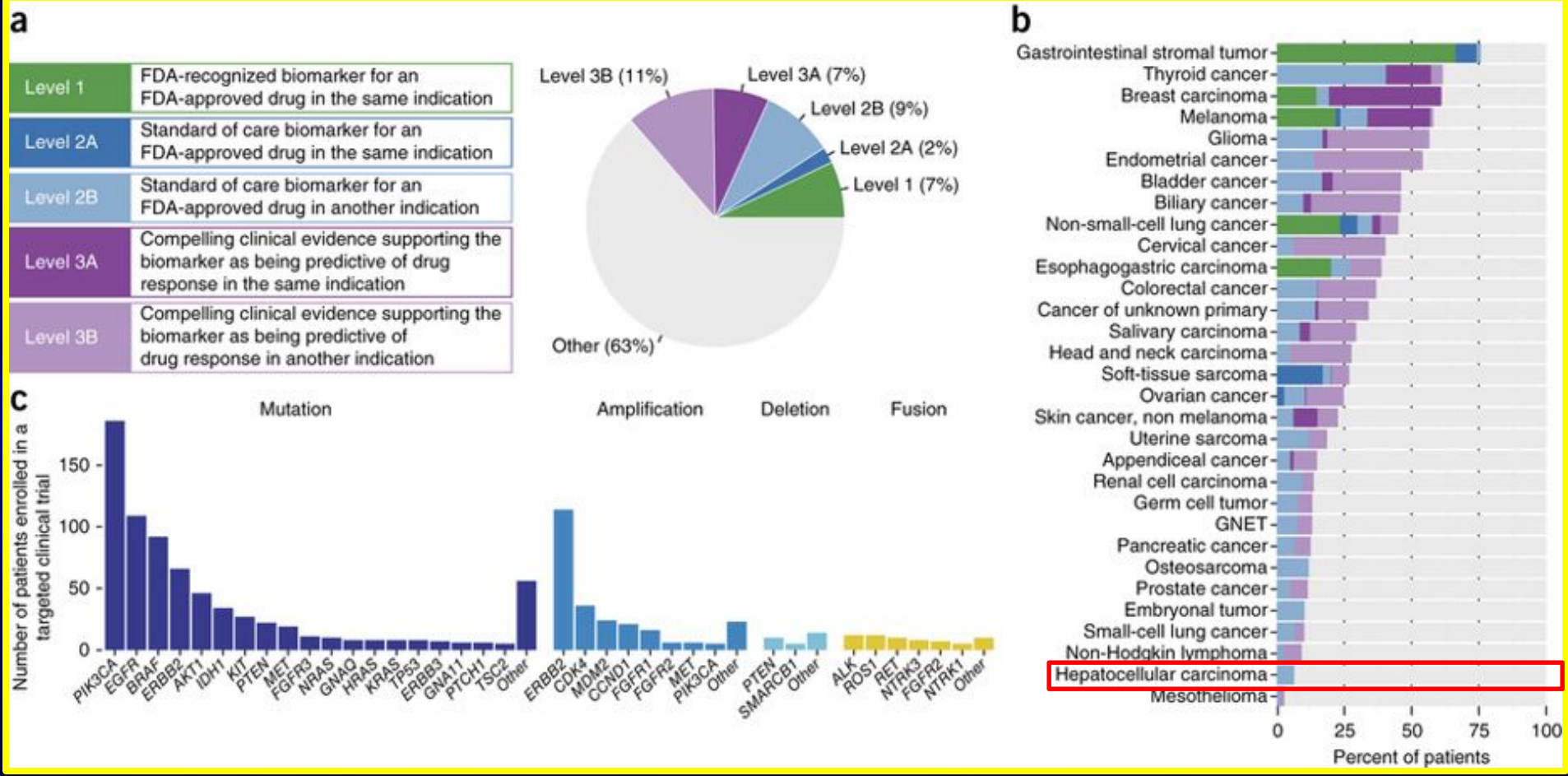
TCGA, Cell June 15th, 2017

HCC -omic Diversity



Uhlen et al. Science 2017

HCC and Targeted Therapy

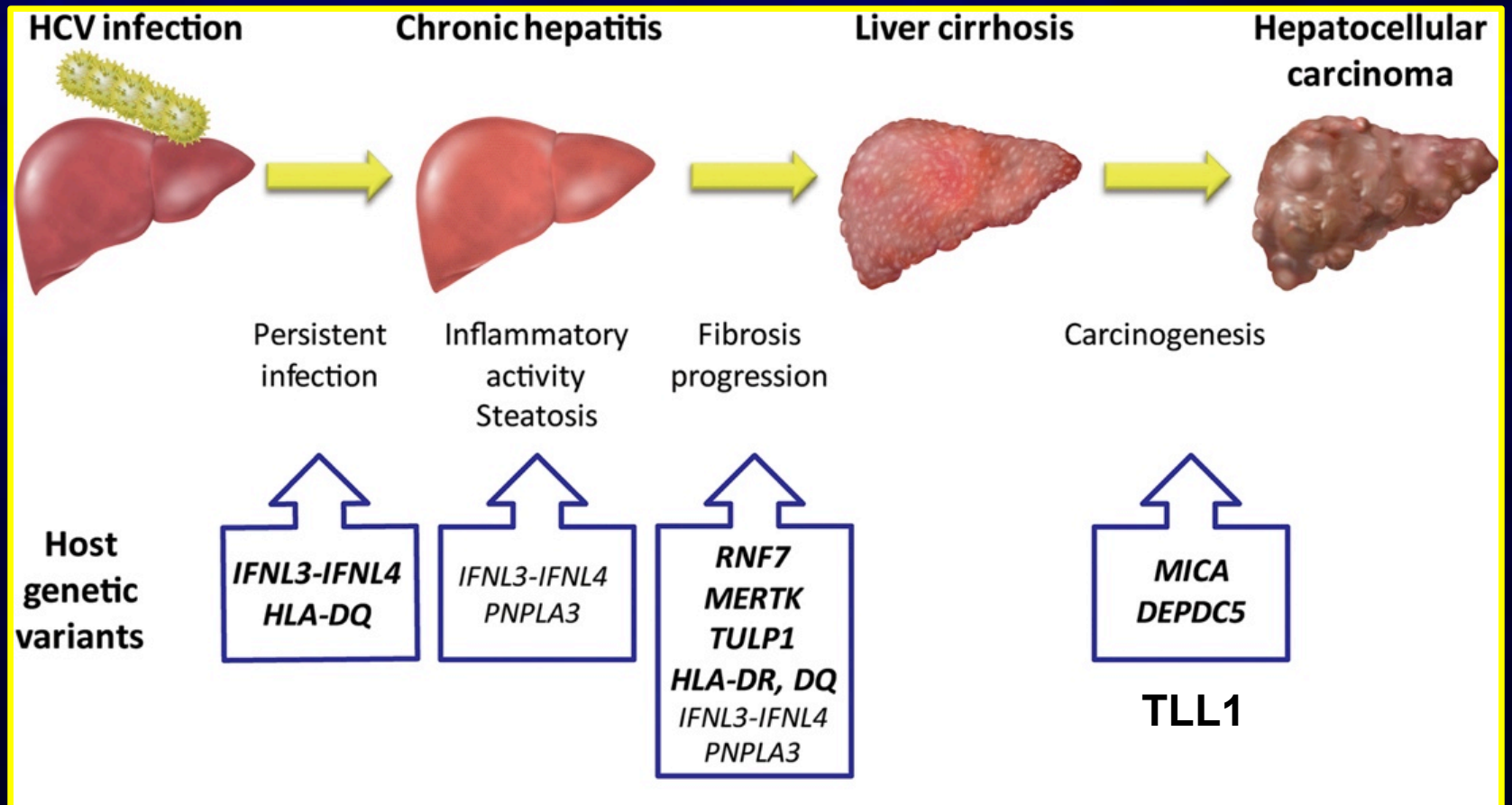


Zehir et al. Nat. Med. 2017 (MSK-IMPACT)

Germline Mutations and HCC

Matsuura & Tanaka Journal of Medical Virology 88:185–195 (2016)

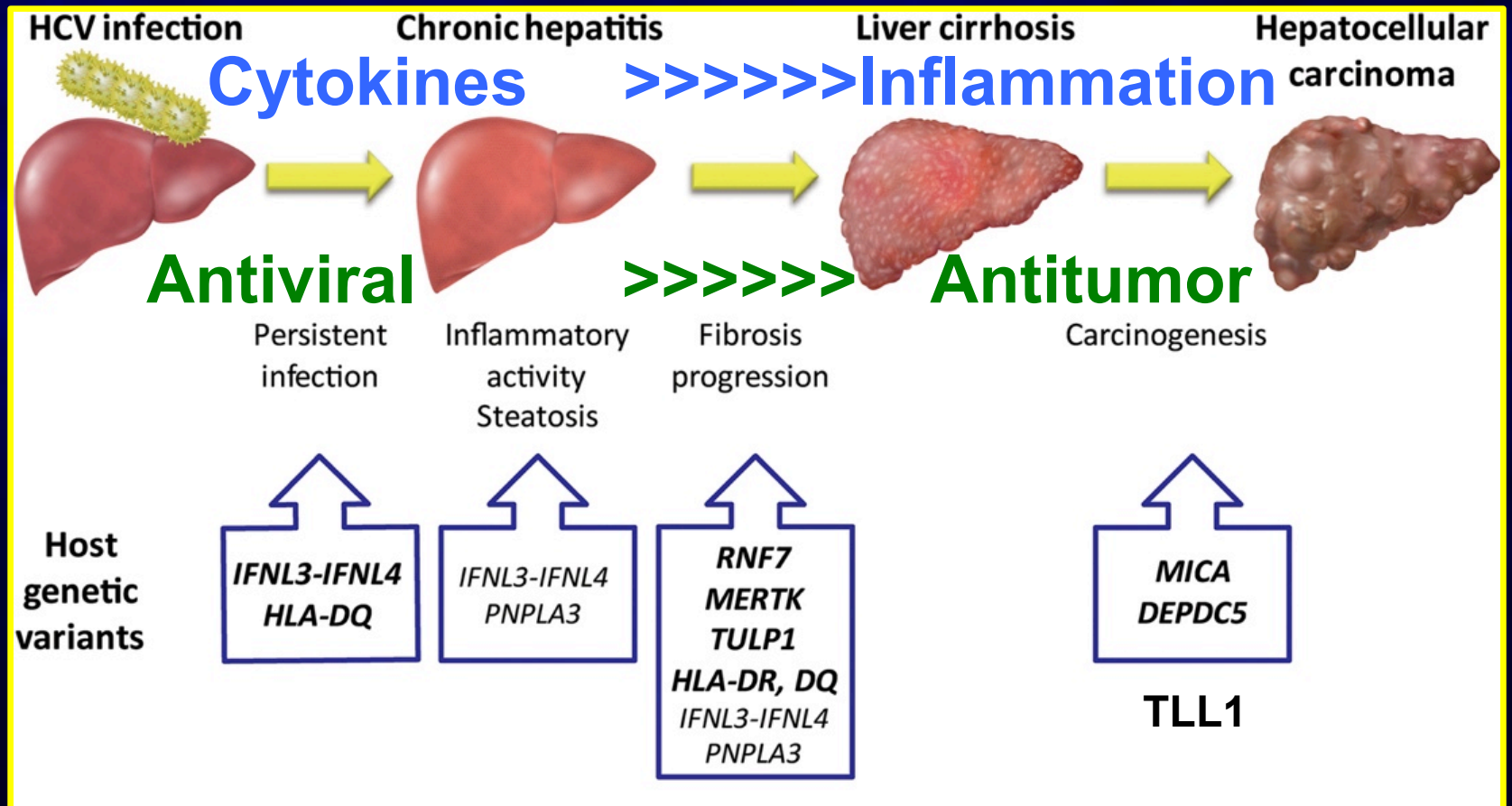
- **Single Nucleotide Polymorphisms (SNPs)**



Novel Genetic Approaches

Matsuura & Tanaka Journal of Medical Virology 88:185–195 (2016)

- **Single Nucleotide Polymorphisms (SNPs)**



Longitudinal Study to Identify Patients with Advancing Liver Disease

Matsuura & Tanaka Journal of Medical Virology 88:185–195 (2016)

- **Single Nucleotide Polymorphisms (SNPs)**

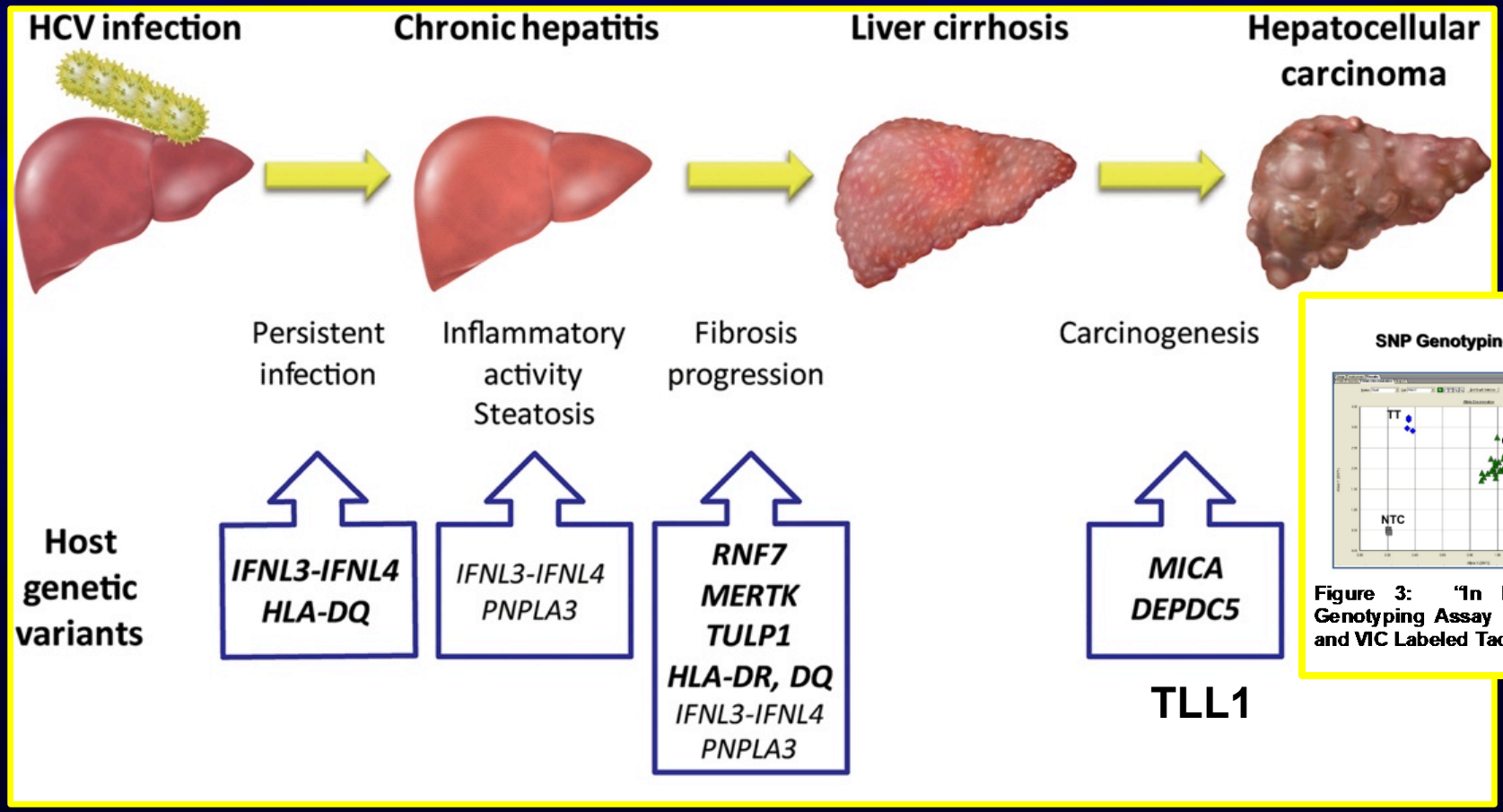
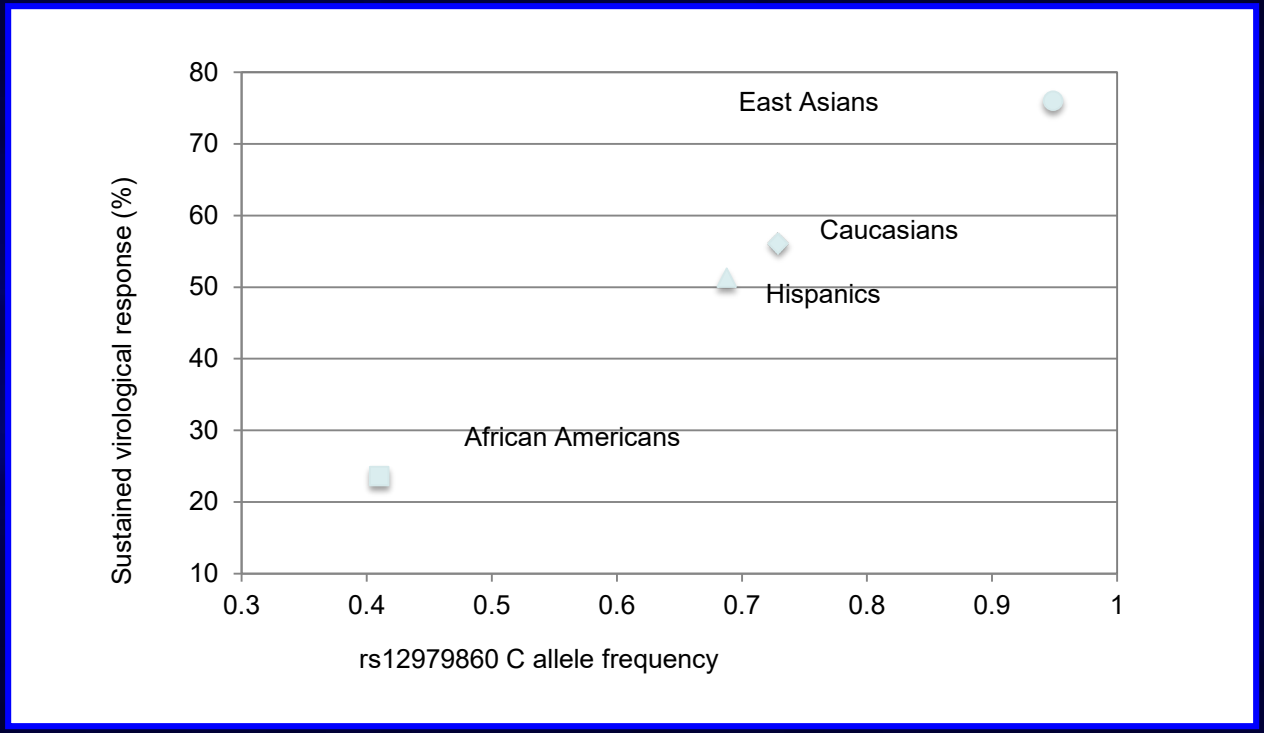


Figure 3: "In House" SNP Genotyping Assay Utilizing FAM and VIC Labeled TaqMan Probes.

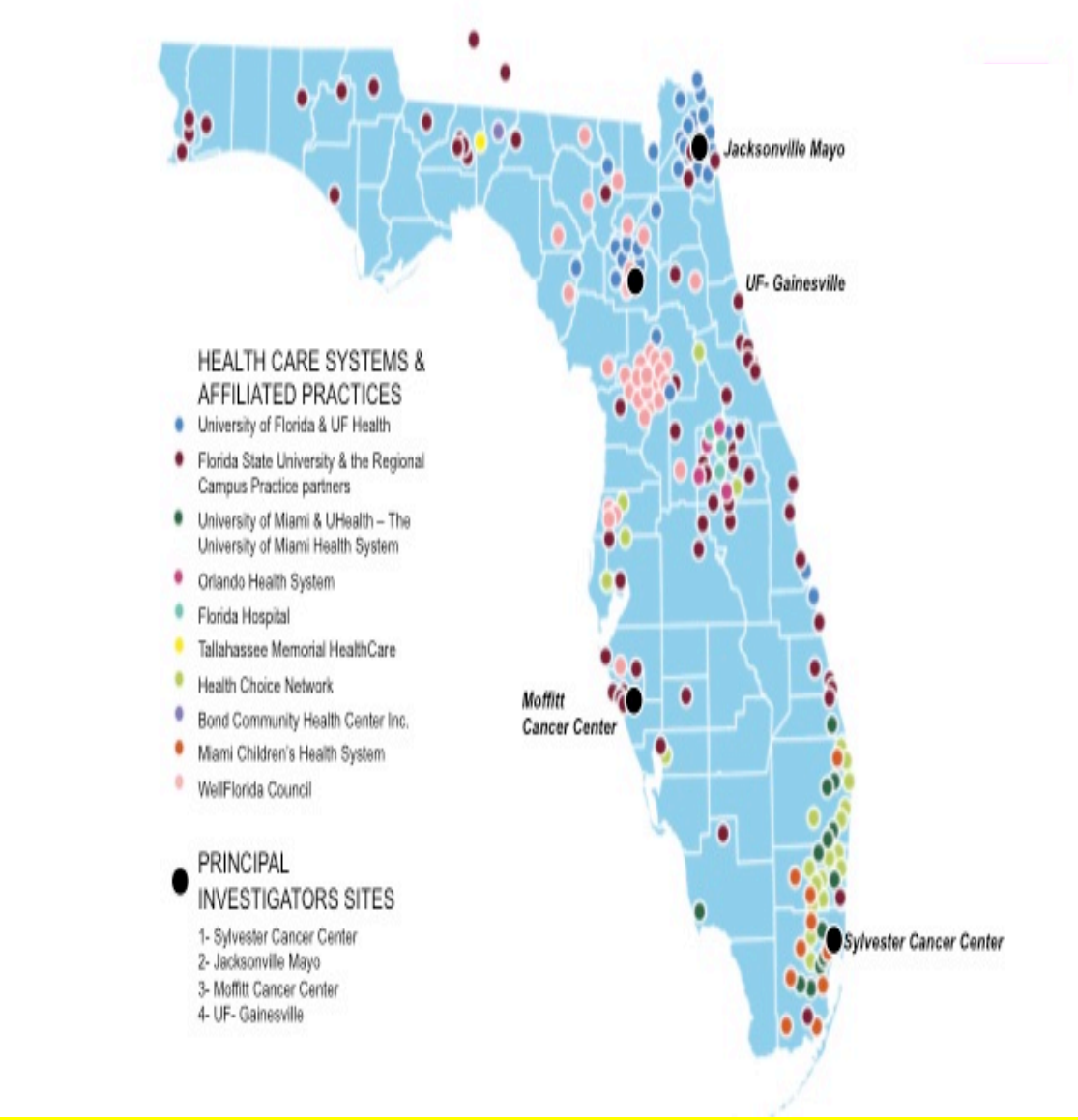
Differences in C allele prevalence contribute the recognized ethnic disparities in SVR rate



~ Half of the difference in SVR between Caucasians and African-Americans could be accounted for by the observed difference in frequency of the C allele

Ge et al, Nature, 2009

Expansion-Statewide Efforts



University of Florida

- David Nelson
- Betsy Shenkman

Moffitt Cancer Center

- Anna Giuliano

Jacksonville Mayo Clinic

- Samuel Antwi

MVA			AUC
	OR	p-value	0.891
AST	0.997	0.1409	
FIB-4 Index	1.293	<.0001	
Fibroscan	1.075	<.0001	
MVA			AUC
	OR	p-value	0.832
AST	0.999	0.6231	
FIB-4 Index	1.043	0.5607	
Est. Fibroscan	1.167	<.0001	

HCC Early Detection Program

- Identify Covariates for HCC Development

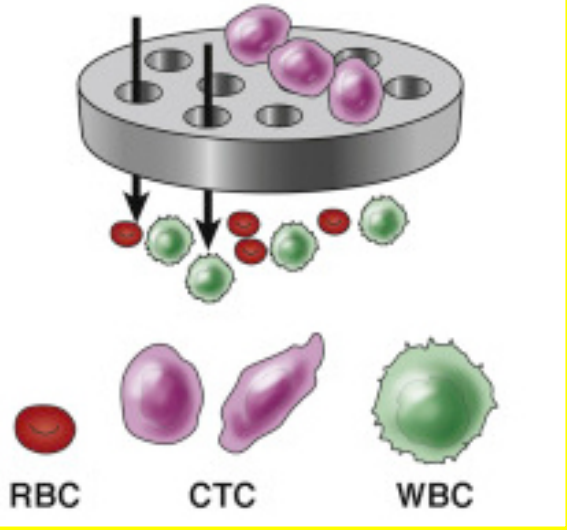
-Prospective, longitudinal study w/ genetic analyses incorporating risk stratification

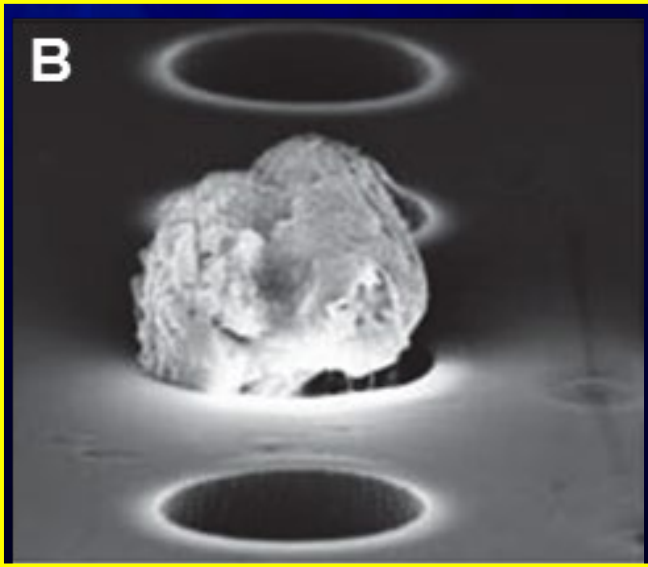
1) Circulating Tumor Cells-CTCs
2) MRI/CT Surveillance (Prediction and Dx)
3) Genomics

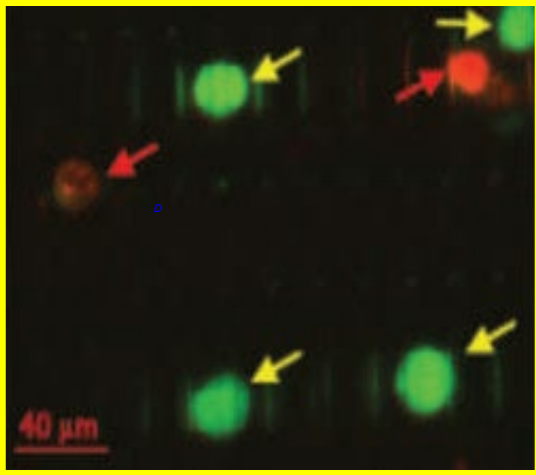
Circulating Tumor Cells: Capture, Enumeration, Analyses

10-100 cells per mL

Cell Type	CTC	Erythrocyte	Leukocyte
Size (μm)	12-25	5-7	7-15

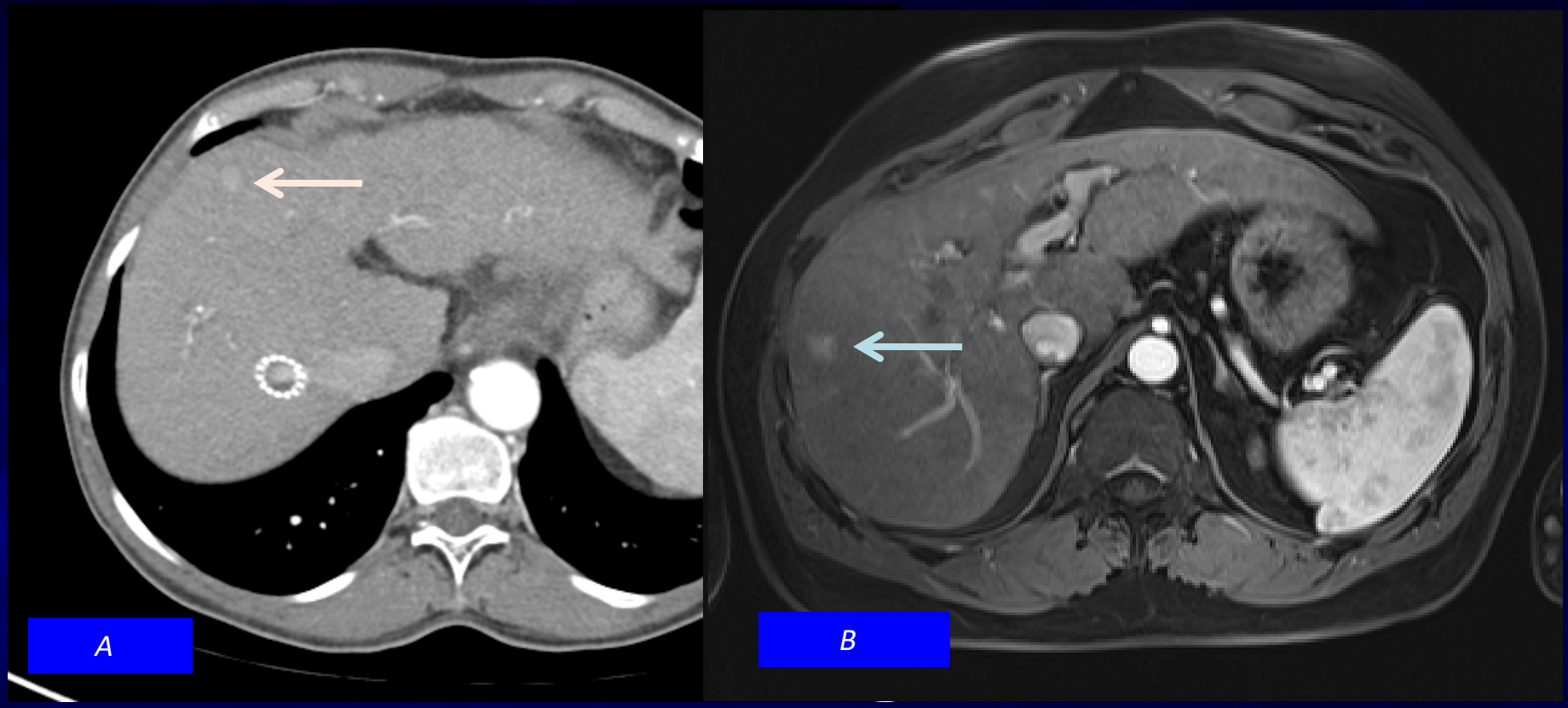






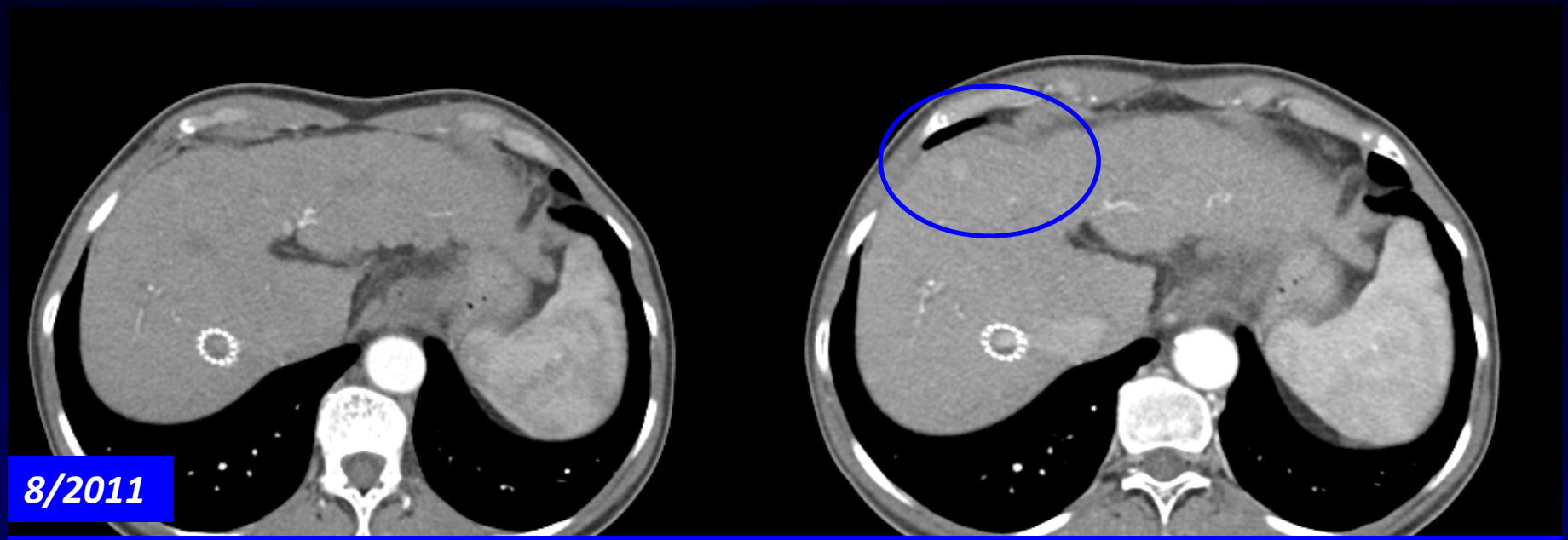
Nagrath et al. 2016, Gastroenterology,

Early Detection of HCC-Imaging

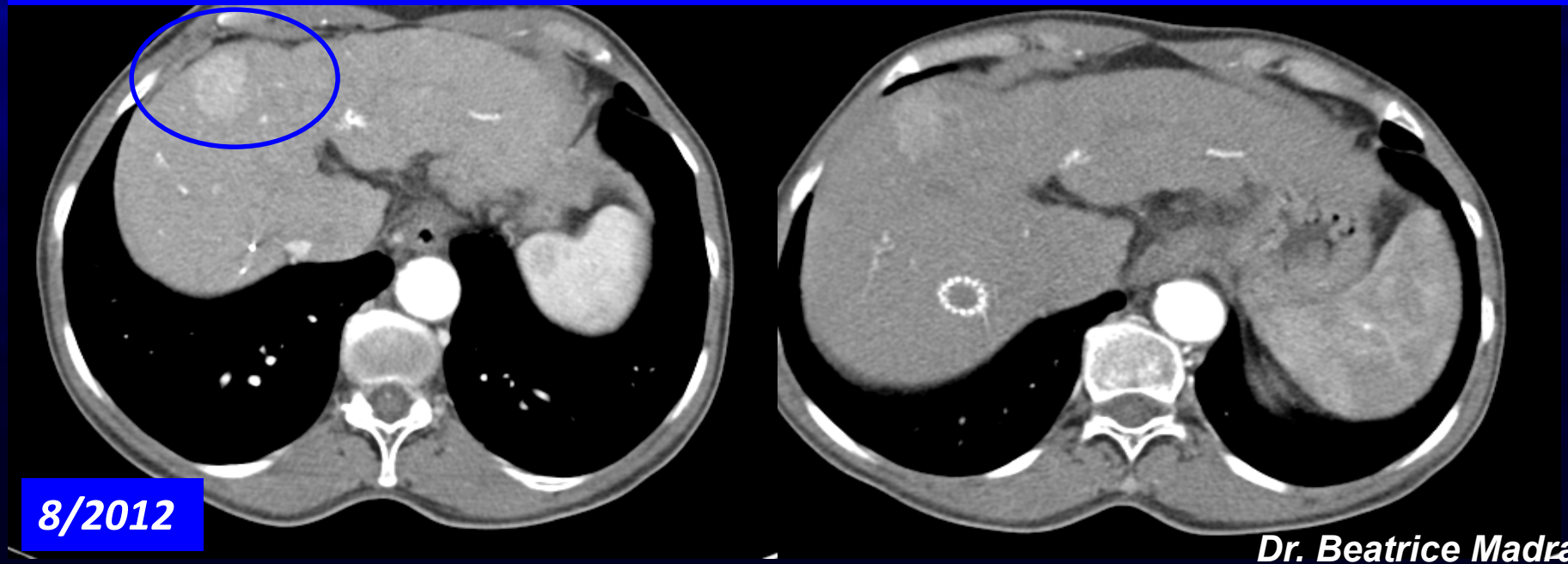


These 2 patients have risk factors for HCC;
these small hypervascularlesions are nearly equal in size.
One of these progressed to HCC.

Dr. Beatrice Madrazo



Patient A of the previous image progressed, in 1 year, from an 8 mms to a 30 mms HCC.



Dr. Beatrice Madrazo

Imaging and Clinical Features of HCC nidus: A Retrospective Study

Madrazo, B[1], Quiroz, AO[2], Santoscoy, JF[3], Pisani, L[1], Serna, MK[4], Casillas, VJ[1], Castillo, RP[1], Kwon, D[5], Martin, EF[1], Thomas, E[5],
[1] University of Miami, Miami, United States [2] Georgetown University, Washington DC, United States, [3]Mount Sinaii Medical Center, Miami Beach, United States, [4]Jackson Memorial Hospital, Miami, United States
[5] Sylvester Comprehensive Cancer Center, Miami, United States

BACKGROUND AND AIMS

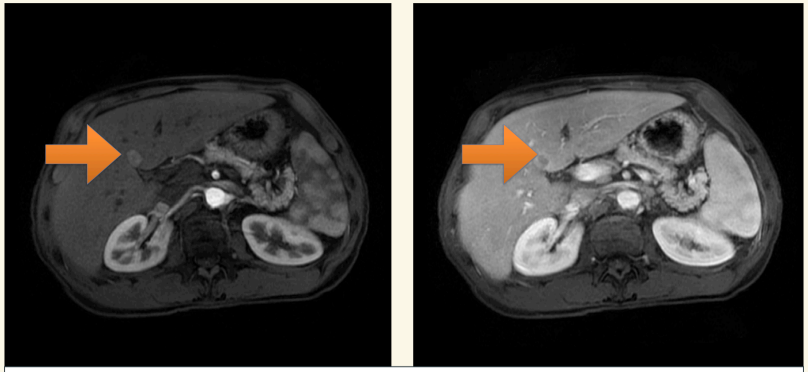
To describe specific imaging findings of early hepatocellular carcinoma (HCC) in correlation with clinical parameters

METHOD

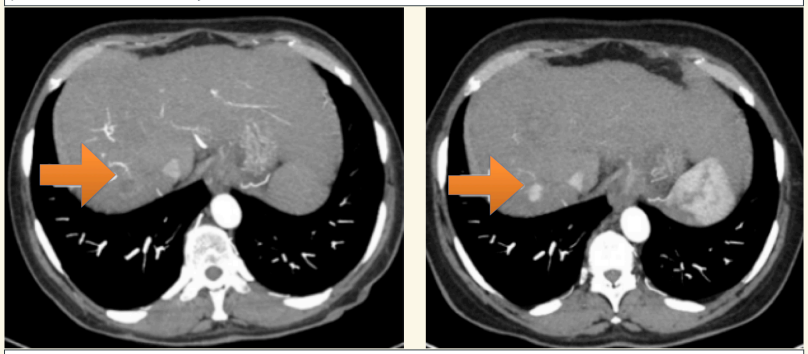
Retrospectively, we reviewed 212 patients with HCC that had a previous imaging study by the time of a perceptible lesion with less than 20mm in size (HCC nidus), and at least one follow-up study after the diagnosis. All clinical data was collected referring to the date of the studies. The study was approved by the ethics committee of the institution.

RESULTS

Of the total, 42 patients (102 studies) met the inclusion criteria and did not have any type of procedure. The cirrhosis type most prevalent was Hepatitis C Virus (HCV) cirrhosis with 24 cases (57.1%), followed by alcoholic (EtOH) cirrhosis (16.6%), Nonalcoholic Steatohepatitis (NASH) disease (9.5%) and combined EtOH and HCV cirrhosis (4.7%). Segment VIII showed to be the most prevalent site of of HCC nidus (26.1%). At the time of a perceptible nidus, AFP level above 20ng/ml was only seen in 4 patients and the overall mean was 9.24ng/ml. A perceptible unpaired hepatic artery suppling the HCC nidus was found in 26.1% of the cases and a capsular artery supply in 3 cases (2.3%). Important findings included HCC nidus do not consistently present complete washout. In our series we only observed complete washout in 33.3% of the patients (14 patients). Mean tumor volume doubling time was 35 months with a range of 1.5 to 842.3 months.

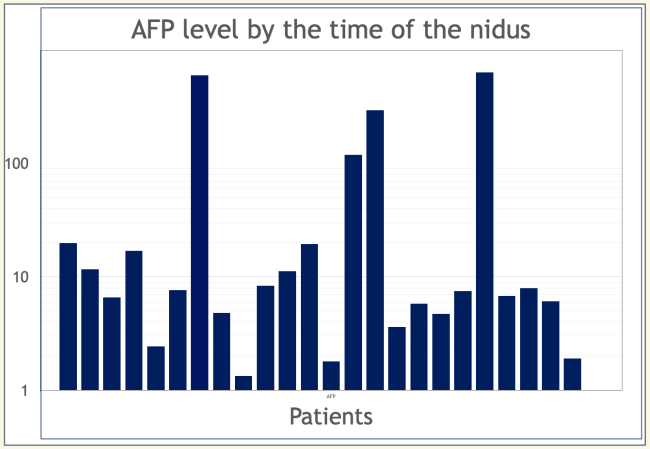


MRI C+ shows lesion <20mm (HCC nidus) with features consistent with LI-RADS 5. There was a total of 6 patients (14.2%) that presented a LIRADS 5 lesion by the time of the nidus.



Contrast enhanced Computed Tomography showing an unpaired hepatic artery supplying the HCC nidus. Unpaired hepatic arteries does not follow the usual directions of the hepatic vasculature. They were present in 26.1% of HCC by the time of the

	EtOH Mean	SD	HCV mean	SD	Other mean	SD	p-value
bmi	28.9	4.11	26.06	3.69	26.55	2.79	0.33
Meld score	8.40	1.15	8.36	1.36	8.55	2.51	0.90
Platelet	64.66	15.01	100.46	36.77	139	52.24	0.01
Albumin	3.03	0.90	3.20	0.52	3.32	0.44	0.85
AFP	2.37	1.14	115.93	180.13	6.01	5.81	0.005



AFP levels above 20 ng/ml was only seen in 4 patients and the overallmeanwas 9.24ng/ml.

Imaging features	n (%)
Homogeneous enhancement	26 (61)
Heterogeneous enhancement	8 (19)
Partial washout	8 (19)
Complete washout	16 (38)
Unpaired Hepatic Artery	11 (26)

CONCLUSION

This study reveals the presence and characteristic of an evolving HCC when the AFP levels are still normal. Platelet count mean and AFP levels mean are significantly greater in the HCV cirrhosis withHCC patients. This reinforces the difference of etiologies of HCC and the role of imaging for earliest detection and undisputed need for screening to provide patients with the best care.

CONTACT INFORMATION

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EASL HCC Meeting
Portugal Nov 2018

HCC Risk Stratification

- **Future Studies**

-Fibroscan CAP score

-ELF

-AFP/L3%/DCP (GALAD & BALAD-2)

-Race/Ethnicity?

-Age Independent Risk?

-F3/Non-Cirrhotic?

Opportunities and Challenges for HIV/HCV ED Screening

1. Increase screening, testing and diagnosis of HCV according to CDC guidelines in public and private healthcare settings (inclusive of younger at risk populations).
2. Build capacity within existing workforce to treat patients in diverse health care environments, including non-specialist settings (i.e. corrections, primary care, addiction medicine, rural healthcare, homeless services, etc.)
3. Ensure access for HCV patients to DAAs [Prescriber and Usage (EtOH/Marij.)]
4. Pursue policies and legislations in alignment with WHO/CDC that will help achieve elimination in FL (Opt-Out Testing, OD Testing, ED reimbursement).

FL- Future Opioid/ID Related Bills

1. Ensure access for HCV patients to DAAs [Prescriber and Usage (EtOH/Marij.)]
2. ED reimbursement
3. Pursue policies and legislations in alignment with WHO/CDC that will help assess the outbreak of viral diseases

-HCV Opt-Out Testing (have lower drug costs now, prisons less of an issue)

-Testing of Unconscious Patient Presenting to ED with Drug Overdose (opioids, cocaine, etc.)

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